

10081806 .060702

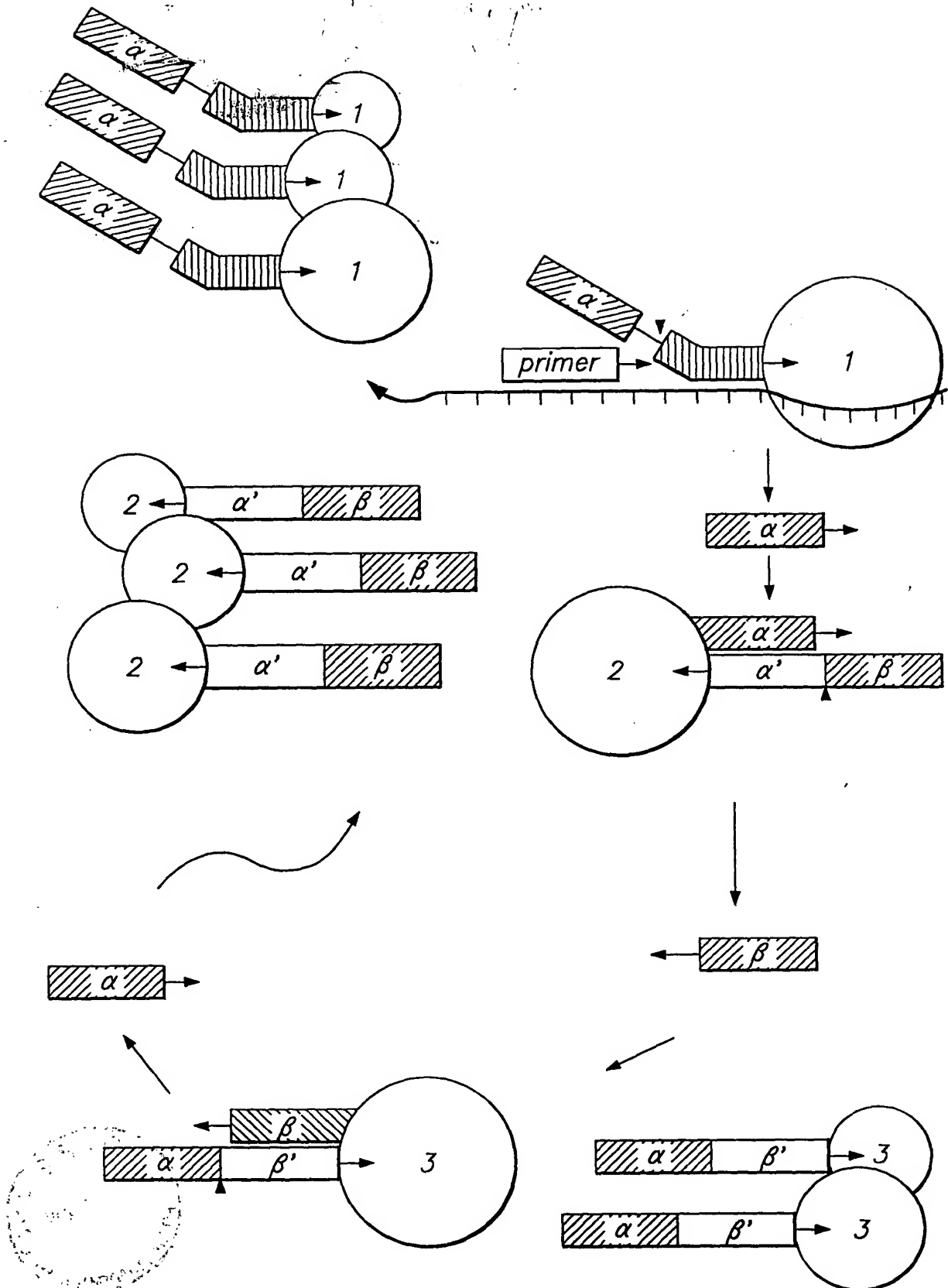


FIG. 1A

complement of α

B-hairpin

5' $c\beta$ 3'

3' α

5' $c\beta$ 3'

3' β

A-hairpin

1 cut

Denature, anneal

First B-hairpin

3' α

5' $c\beta$ 3'

3' β

Cleaved A-hairpin

Denature, anneal

Second molecule of A-hairpin

5' α

5' $c\beta$ 3'

3' β

2 cuts

Cleaved B-hairpin

B-hairpins

3' α

3' β

4 cuts

Cleaved A-hairpins

A-hairpins

```

MAJORITY ATGXXGGCGATGCTTCCCTCTTTGAGCCCAAGGCCGGGTCTCTCTGGTGGACGGGCACCTGGCCT
DNAPTAQ   .AG..G.....G..... 70
DNAPTFL   .....C.G..... 67
DNAPTTH   .GA.....G.....A..... 70
MAJORITY ACCGCACCTTCTTCGCCCTGAAGGCCCTCACCACCACCCOGGGGGAACCGGTGCAGGGGTCTACGGCTT
DNAPTAQ   .....CA.....G..G..... 140
DNAPTFL   .....T.....C.....C..T..... 137
DNAPTTH   .....G..... 140
MAJORITY CGCCAAGAGCCTCCTCAAGGCCCTGAAGGAGGACGGGGACXXGCCGGTGXTCGTGCTTTGACGCCAAG
DNAPTAQ   .....C.....A..... 207
DNAPTFL   .....A.....GT..T..... 204
DNAPTTH   .....T..AA..C..CT..... 280
MAJORITY GCCCCTCCTTCGCGCCACGAGGCCTACGAGGCCTACAAGCGGGCGGCCACCCCGGAGGACTTTC
DNAPTAQ   .....G..GG.....G..... 277
DNAPTFL   ..... 274
DNAPTTH   .....GA.....G.....C..... 280
MAJORITY CCCGGCAGCTCGCCCTCATCAAGGAGCTGGTGGACCTCCTGGGGCTTGCGCGCCTCGAGGTCCCCGGGCTA
DNAPTAQ   .....A.....G..... 347
DNAPTFL   .....G.....T.....A..C.....T..G..G.....T 344
DNAPTTH   ..... 350

```

FIG.2A

MAJORITY CGAGGCGGACGACGTGCTGGCCACCTGTGCCAAGAGCGGAAAGGAGGGGTACGAGGTGCGCATCCTC

DNAPTAQC.....G.....C.....C..... 417
 DNAPTFL T.....G.....CG..... 414
 DNAPTTHT.C..... 420

MAJORITY ACCGCCGACCGGACCTCTACCAGCTCCTTTCCGACCGCATCGCCGTCTCCACCCCGAGGGGTACCTCA

DNAPTAQAAA.....T.....CA..... 487
 DNAPTFLT.....G.G.....A.....T.....G. 484
 DNAPTTHA.G.C.....G.....CC..... 490

MAJORITY TCACCCCGGCGTGGCTTTGGGAGAAGTACGGCCTGAGGCCGGAGCAGTGGGTGGACTACCGGGCCCTGGC

DNAPTAQC.....A.....C.C.....CC.....A. 557
 DNAPTFLAC.....C.C..... 554
 DNAPTTHA.....C.....T.C.....C.T 560

MAJORITY GGGGGACCCCTCCGACAACTCTCCCGGGGTCAAGGGCATCGGGGAGAGACCGCCXGAAGCTCCTCXAG

DNAPTAQ C.....GAG.....T.....G.GAG.....T..GG.. 627
 DNAPTFLG.T..A.....G.....A.G...A..CGC 624
 DNAPTTHTC.....A.. 630

MAJORITY GAGTGGGGGAGCCTGGAAACCTCTCAAGAACCTGGACCGGGTGAAGCCCGC...CXTCCGGGAGAAGA

DNAPTAQGC.....C.....A..... 694
 DNAPTFLT.C.C.....A.....T....T.G.....C 691
 DNAPTTHA.....A.....A.AAA.G..... 700

FIG. 2B

MAJORITY TCCAGGGCCACATGGAXGACCTGAXGCTCTCCTGGGAGCTXTCCAGGTGCGCACCGACCTGCCCTCTGGA

DNAPTAQC..T...A.....C..GG..A..... 764
 DNAPTFLGGG.....G.C...GCC..T...C..A...T...A...T... 761
 DNAPTTHC.....A.....C.G.....T.....C.....C..... 770

MAJORITY GGTGGACTTCGCCAAGXGGCGGGAGCCCCGACCGGGAGGGGCTTAGGGCCTTTCTGGAGAGGCTGGAGTTT

DNAPTAQAA.....AA.....A.....T.....T..... 834
 DNAPTFLGG.G.C.C..CACA...A...T.....T..GC...T...T...C..T... 831
 DNAPTTHC.....C..G.....C.....C.....C.....C..... 840

MAJORITY GGCAGCCTCCTCCACGAGTTTCGGCCTCTCTGGAGGGCCCCAAGGCCCTGGAGGAGGCCCTGGCCCCCGC

DNAPTAQT.....AA..... 904
 DNAPTFLA.....G.....G...G.GCA.....T... 901
 DNAPTTHC.....C.....GCCC..... 910

MAJORITY CGGAAGGGGCTTCGTGGGCTTTGTCTCTTCCCGCCCCGAGCCCATGTGGGCCGAGCTTCTGGCCCCCTGGC

DNAPTAQT.....G.....AAG.....T..... 974
 DNAPTFLT..TT.....TC.T.....T..... 971
 DNAPTTHC.....C.....G.....AAA..... 980

MAJORITY CGCCGCCAGGGAGGGCGGGTCCACCGGGCACCAGACCCCTTTAXGGGCCTXAGGGACCTXAAGGAGGTG

DNAPTAQG.....C..C..G..T.A..AA.C...C.....G.....C. 1044
 DNAPTFL T.GG..GT.....G..CC.....T.....A.....C...G.....G.....T...G.... 1041
 DNAPTTHTG.....C.....G.....G.....GGC...G..A..A.....C.....C 1050

FIG. 2C

| | | |
|----------|---|------|
| MAJORITY | CGGGGXCTCCTCGCCCAAGGACCTGGCCGTTTTTGGCCCTGAGGGAGGCCTXGACCTCXTGCCCGGGGACG | |
| DNAPTAQ |G..T.....A.....AG.....C.....A.....T.G.....CC.....C..... | 1114 |
| DNAPTFL |AA.....G.....G.....C.....G.....T.C.....A.A..... | 1111 |
| DNAPTTH |C.....C.....TC.....G.A.....G..... | 1120 |
| MAJORITY | ACCCCATGCTCCTCGCCTACCTCCTGGACCCCTCCAACACCACCCCGAGGGGTGGCCCGGCTACGG | |
| DNAPTAQ |T..... | 1184 |
| DNAPTFL |G.....T.....T.....T..... | 1181 |
| DNAPTTH |G.....G..... | 1190 |
| MAJORITY | GGGGGAGTGACGGAGGAXGCGGGGAGCGGGCCCTCCTXTCCGAGAGGCTCTTCCXGAACCTXXXGGAG | |
| DNAPTAQ | C.....G.....GC..T.....GCC.....GTG..G. | 1254 |
| DNAPTFL |T.....A.....GG.....C.C.....A.C...AAA.... | 1260 |
| DNAPTTH |C.C.CCC.C.....C.G.....CAT.G.....CCTTA.. | 1260 |
| MAJORITY | CGCCTTGAGGGGAGGAGGCTCCTTTGGCTTTACCAGGAGGTGGAGAAGCCCTTTCCCGGGTCCICGG | |
| DNAPTAQ | A.G.....G.....G.....G.....GCT..... | 1324 |
| DNAPTFL |A...A..A..AC.C..G.....G.....G.....GT... | 1321 |
| DNAPTTH |C.....A.....C.....C.....A.....C..... | 1330 |
| MAJORITY | CCACATGGAGGCCACGGGGGTXCGGCTGGACGTGGCCTACCTCCAGGCCCTXTCCCTGGAGGTGGCGGA | |
| DNAPTAQ |G..C.....T...AG....T.G.....C... | 1394 |
| DNAPTFL |GG.....C.....C.....C.....A..C | 1391 |
| DNAPTTH |C.....A.....T.....T.....C.T..... | 1400 |

FIG.2D

| | | |
|----------|--|------|
| MAJORITY | GGAGATCCGCCGCTCGAGGAGGAGGTCTTCCGCCTGGCCGGCCACCCCTTCAACCTCAACTCCCGGGAC | |
| DNAPTAQ |GC.....CC..... | 1464 |
| DNAPTFL |G.G....AG..G..... | 1461 |
| DNAPTTH |T.....G..... | 1470 |
| MAJORITY | CAGCTGGAAAGGGTGCTCTTTGACGAGCTXGGGCTTCCCGCCATCGGCAAGACGGAGAAGACXGGCAAGC | |
| DNAPTAQ |C.....A..... | 1534 |
| DNAPTFL |GC.....G.C..G..T..... | 1531 |
| DNAPTTH |TA.....T.G..G.....C.A..... | 1540 |
| MAJORITY | GCTCCACGAGCGCCGCTGCTGGAGGCCCTXCGXGAGGCCACCCCATCGTGGAGAAGATCCTGCAGTA | |
| DNAPTAQ |C.....C.C..... | 1604 |
| DNAPTFL |T.....G..A.....CCGC..... | 1601 |
| DNAPTTH |G.....A..G.....C...C..... | 1610 |
| MAJORITY | CCGGGAGCTCACCAAGCTCAAGAACACCTACATXGACCCCTGCCXGXCCTCGTCCACCCACGGACGGGC | |
| DNAPTAQ |G....G.....T.....T....G.A...A..... | 1674 |
| DNAPTFL |A.....C.C...G.....A...C...C... | 1671 |
| DNAPTTH |G.G.....AAG.....G..... | 1680 |
| MAJORITY | CGCCTCCACACCCGCTTCAACCAGACGGCCACGGCCACGGGAGGCTTAGTAGCTCCGACCCCAACCTGC | |
| DNAPTAQ |A.....T.....C..... | 1744 |
| DNAPTFL |G.....C.....TCC..... | 1741 |
| DNAPTTH |G.....G..... | 1750 |

FIG. 2E

```

MAJORITY AGAATATCCCGTCCGCACCCXCTGGCCAGAGGATCCGCCGGGCTTCGTGGCCGAGGAGGGXTGGGT
DNAPTAQ .....G..T..G.....A..C.....G...C.. 1814
DNAPTFL .....G.....T.....C..C.....A.....C..... 1811
DNAPTTH .....CT.....C.....T.....C..... 1820
MAJORITY GTTGGTGGCCCTGGACTATAGCCAGATAGAGCTCCGGGTCTCGGCCACCTCTCCGGGGACGAGAACCTG
DNAPTAQ A.....A.....A.....G.....C..... 1884
DNAPTFL .C.....T..T.....C.....T.....T..... 1881
DNAPTTH .....C.....C.....C.....A..... 1890
MAJORITY ATCCGGGTCTTCCAGGAGGGAGGACATCCACACCCAGACCGCCAGCTGGATGTTCCGGCGTCCCCCCCGG
DNAPTAQ .....C.....C.....GG.....G... 1954
DNAPTFL .....T.....T.....TT.....C.. 1951
DNAPTTH .....A.....A.....A..... 1960
MAJORITY AGGCCGTGGACCCCTGATGCGCCGGCGGCCAAGACCATCAACTTCGGGGTCTCTACGGCATGTCGGC
DNAPTAQ .....G... 2024
DNAPTFL .A.GG..A...T.....G..... 2021
DNAPTTH .....GG.G.....C..... 2030
MAJORITY CCACCGCCTCTCCAGGAGCTTGCCATCCCCCTACGAGGAGGGCGGTGGCCTTCATTGAGCGCTACTTCCAG
DNAPTAQ .....A.....T.....CCA.....T... 2094
DNAPTFL .....GG.....T..... 2091
DNAPTTH ...TA.G.....T..A.....A 2100

```

FIG. 2F

| | | |
|----------|--|------|
| MAJORITY | AGCTTCCCCAAGGTGCGGCCTGGATTGAGAAAGACCCTGGAGGAGGCAGGAGGCGGGGTACGTGGAGA | |
| DNAPTAQ | | 2164 |
| DNAPTFL | ...A.....GG.....C.....C.CC.....T..... | 2161 |
| DNAPTTH |A.A.....G.....A.....C.....A..... | 2170 |
| MAJORITY | CCCTCTTCGGCGCCGGCTACGTGCCCGACCTCAACGCCCGGGTGAAGAGCGGTGCGGAGGCGGCGGA | |
| DNAPTAQ |C.....A.....AG.G.....C..... | 2234 |
| DNAPTFL |T.....C..... | 2231 |
| DNAPTTH | ...AA.AA.....CA.....C..... | 2240 |
| MAJORITY | GCGCATGGCCTTCAACATGCCCGTCCAGGGCACCGCCGACCTCATGAAGCTGGCCATGGTGAAGCTC | |
| DNAPTAQ | | 2304 |
| DNAPTFL |G.....T.....CG...T | 2301 |
| DNAPTTH |C..... | 2310 |
| MAJORITY | TTCCCCCGGCTXCAGGAAATGGGGGCCAGGATGCTCTXCAGGTCCACGACGAGCTGGTCTCTCGAGGCCCC | |
| DNAPTAQ |A...GG.....T..... | 2374 |
| DNAPTFL |T...C.....G.....TT.G.....G..... | 2371 |
| DNAPTTH |C.C.G...G.....C.C.....C.....CC...G..... | 2380 |
| MAJORITY | CCAAAGAGCGGGCGGAGGXGGTGGCCCGCTTTGGCCCAAGGAGGTTCATGGAGGGGGTCTATCCCCCTGGCCGT | |
| DNAPTAQ | A.....A.....CC.....CGGC.....G..... | 2444 |
| DNAPTFL | ...G..C.....AG...A.....GG.....CAG.. | 2441 |
| DNAPTTH | .C...C.....C...A.....G.....C.....AA..C.....C..... | 2450 |

FIG. 2G

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MAJORITY G C C C C T G G A G G T G G G G A T G G G G G A G G A C T G G C T C T C C G C C C A A G G A G T A G

| | | |
|---------|------------------|------|
| DNAPTAQ |A.....GA | 2499 |
| DNAPTFL |CC..... | 2496 |
| DNAPTTH |T.....GT... | 2505 |

FIG. 2H

| | | |
|----------|--|-----|
| MAJORITY | MXAMLPLFEPKGRVLLVDGHHLAYRTFFALKGLTTSRGEVPQAVYGFAKSLLKALKEDG·DAVXVVVFDK | |
| TAD PRO | RG.....H.....I..... | 69 |
| TFL PRO |V.V..... | 68 |
| TTH PRO | E.....YK..F..... | 70 |
| MAJORITY | APSRHEAYEAYKAGRPTPEDFROLALIKELVDLLGLXRLEVPGYEADDVLTATLAKAEKEGYEVRI | |
| TAG PRO | GG.....A.....S..... | 139 |
| TFL PRO |V.....F.....R..... | 138 |
| TTH PRO |FT..... | 140 |
| MAJORITY | TADRDLQLLSDRIAHLHPEGYLITPAWLWEKYGLRPEQWVDYRALXGDPDSNLPVGKIGEKTA | |
| TAG PRO | K.....H.....D.A.....T.E.....R...E | 209 |
| TFL PRO |E...I.....Y.....A.....I.....QR..IR | 208 |
| TTH PRO | V...V.....H...E.....F...V.....L...K | 210 |
| MAJORITY | EWGSLENLLKNLDRVKP·XXREKIXAHMEDLXLSSXLSXVRTDLPLEVDFAXRREPDRGLRFLERLEF | |
| TAG PRO | A.....L...AI...L...D..K..WD.AK.....K.....R..... | 278 |
| TFL PRO | FQH...Q...SL...LQ.G..A.A..RK..Q.H.....GR..T.NL..... | 277 |
| TTH PRO | ENV.....K..L...R..LE..R.....L.QG..... | 280 |
| MAJORITY | GSLLEFGLLXPKALEEAPWPPPEGAFVGFVLSRPEPMWAEELLALAAARXGRVHRAXDPLXGLRDLKEV | |
| TAG PRO | S.....K.....D.....PE.YKA.....A | 348 |
| TFL PRO | G...A.....L..SF.....G.WE..L...Q...R.....G. | 347 |
| TTH PRO | A.AP.....K.....C.D.....A...A..K..... | 350 |

FIG. 3A

| | | |
|----------|--|-----|
| MAJORITY | RGLAKDLAVLALREGDLXPGLDPMLLAYLLDPSNTTPEGVARRYGGWETEDAGERALLSERLFXNLXX | |
| TAQ PRO |S.....G.P.....E.....A.....A.....A..WG | 418 |
| TFL PRO |I.....F.E.....A.....QT.KE | 417 |
| TTH PRO |S.....V.....AH.....HR..LK | 420 |
| MAJORITY | RLEGEERLLWLYXEVEKPLSRVLAHMEATGVRLDVAYLQALSLEVAEEIRRLLEEVEFRLAGHPFNLSRD | |
| TAQ PRO |R..R..A.....R.....A.....A..... | 488 |
| TFL PRO |K.....E.....R.....EA.V.Q..... | 487 |
| TTH PRO |K.....H.....L..... | 490 |
| MAJORITY | QLERVLFDELGLPAIGKTEKTKRSTSAAVLEALREAHPIVEKILQYRELTKLKNITYIDPLPXLVHPRTG | |
| TAQ PRO |R.....L.....Q.....H.....V.....S..... | 558 |
| TFL PRO |R.....L.....Q.....H.....V.....S..... | 557 |
| TTH PRO |R.....L.....Q.....H.....V.....S..... | 560 |
| MAJORITY | RLHTRFNQTATGRLSSSDPNLQNIPTPLGQIRRAFVAEEGWXLVALDYSQIELRVLAHLSGDENL | |
| TAQ PRO |I.....L..... | 628 |
| TFL PRO |V.....V..... | 627 |
| TTH PRO |A.....A..... | 630 |
| MAJORITY | IRVFQEGRDIHTQTASWMFGVPPEAVDPLMRRAAKTINFGVLYGMSAHRLSQELAIPYEEAVAFIERYFQ | |
| TAQ PRO |E.....R.....Q..... | 698 |
| TFL PRO |S.G.....G.S..... | 697 |
| TTH PRO |K.....V..... | 700 |

FIG. 3B

MAJORITY SFPKVRWIEKTLLEGGRRRGYVETLFGRRRYVPDLNARVKSAREAAERMAFNMPVQGTAAADLMKCLAMVKL

| | | |
|---------|--------------|-----|
| TAQ PRO |E..... | 768 |
| TFL PRO | Y.....G..... | 767 |
| TTH PRO |K..... | 770 |

MAJORITY FPRLXEMGARMLLQVHDELVLAPKXRAEXVAALAKEVMEGVYPLAVPLEVEVGXGEDWLSAKEX

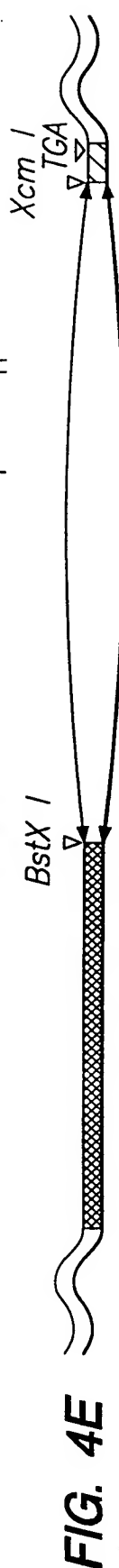
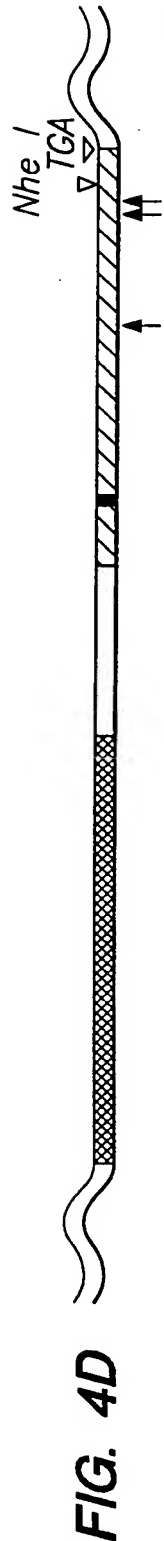
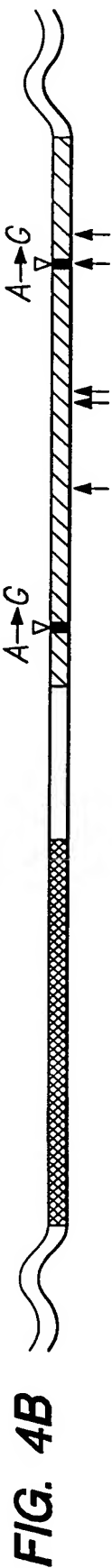
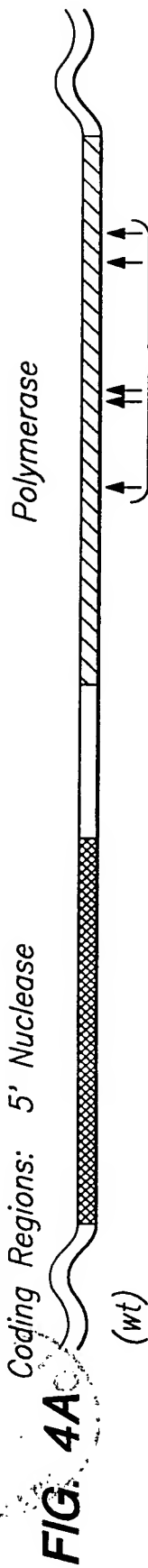
| | | |
|---------|--|-----|
| TAQ PRO |E.....E...A..R.....I..... | 833 |
| TFL PRO |Q..L.....D...R.....W..Q.....L..... | 831 |
| TTH PRO |R.....L....QA...E.....A..KA.....M.....G | 835 |

FIG. 3C

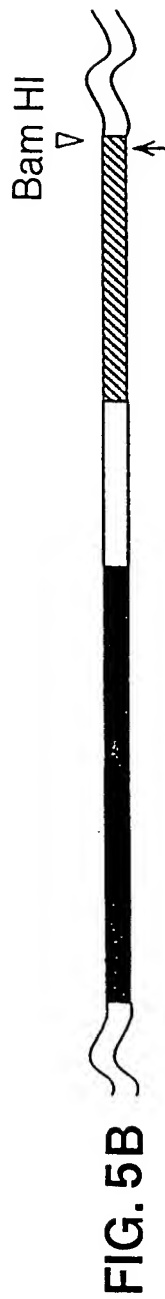
Genes for Wild-Type and Pol(-)DNAPTaq

Domain

Coding Regions: 5' Nuclease



Genes for Wild-Type and Pol(-)DNAPTfl



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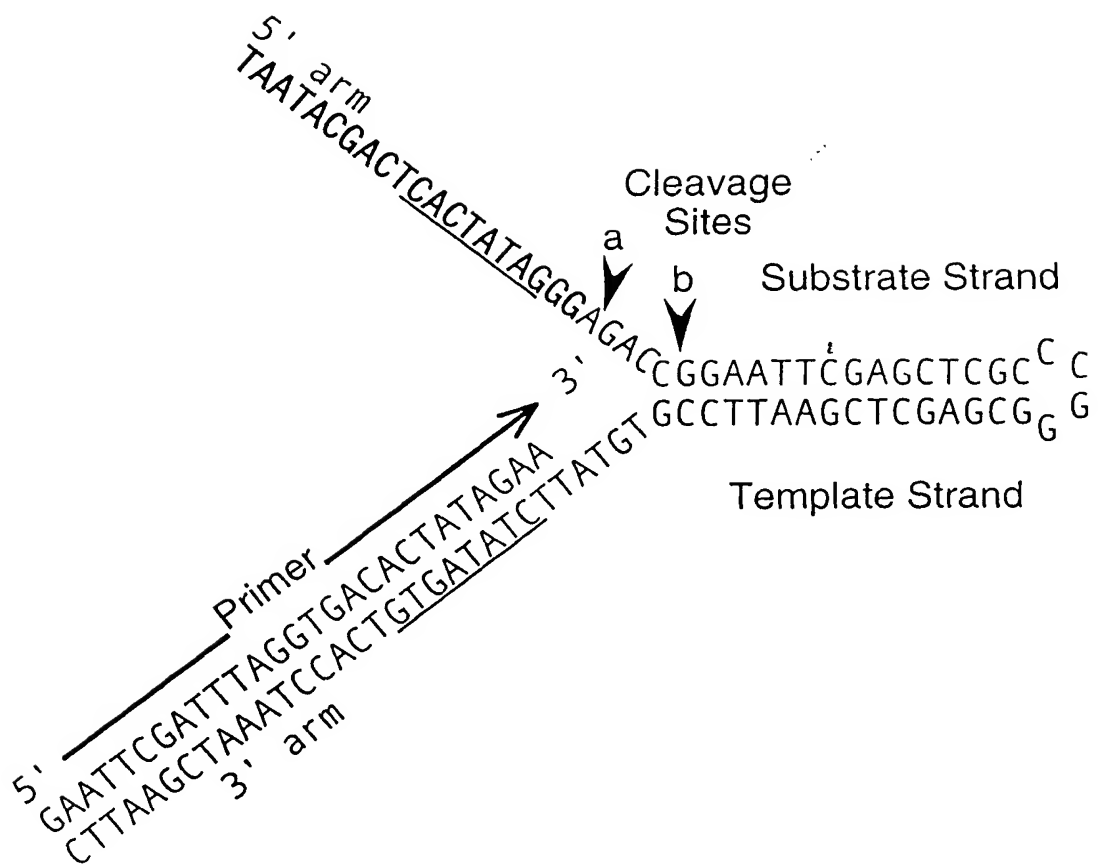


FIG. 6

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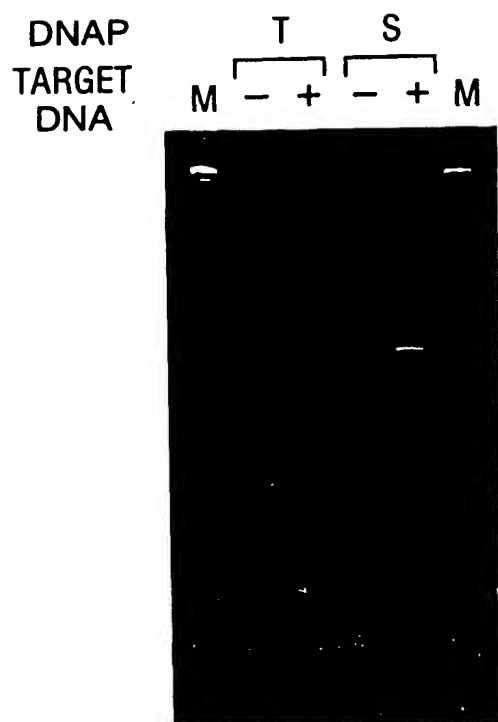


FIG. 7



10004306-060702

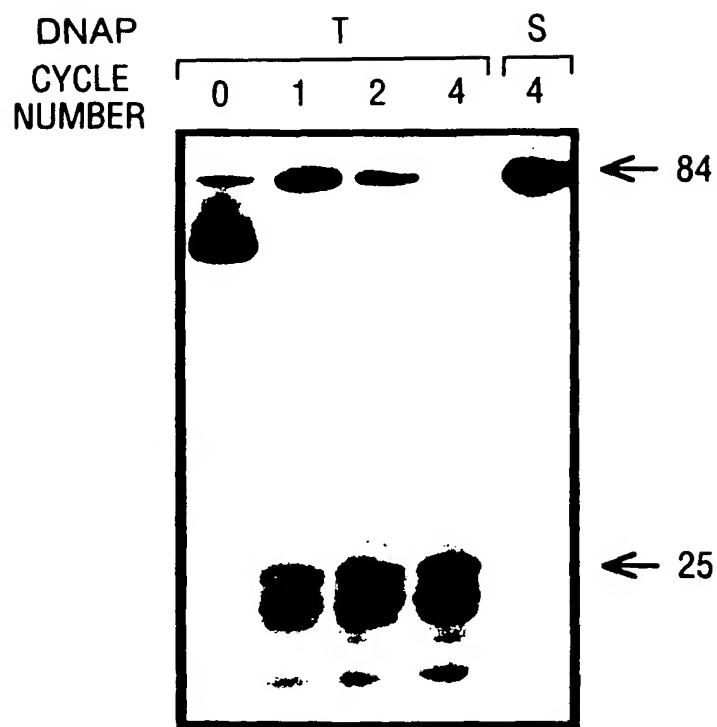
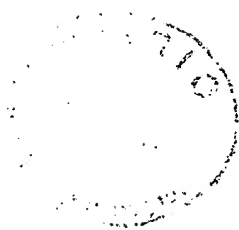


FIG. 8



| | 1 | 2 | 3 | 4 | 5 | 6 |
|--------------------------|---|---|---|---|---|---|
| DNAP-T: | - | + | + | + | + | + |
| MgCl₂: | + | - | + | + | + | + |
| dNTPs: | + | - | + | - | + | - |
| Primers: | + | - | + | + | - | - |

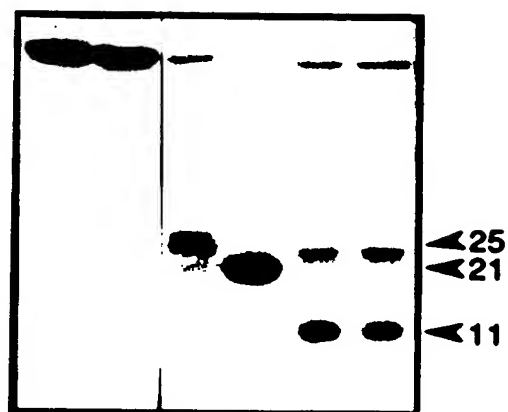
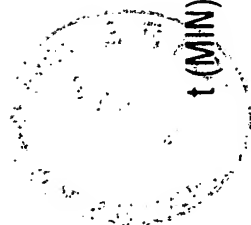


FIG. 9B

204090* 908T800F



+ PRIMER
M 0 0.5 1 3 5 10 M
- PRIMER
M 0 5 10 20 40 60 M



FIG. 10A

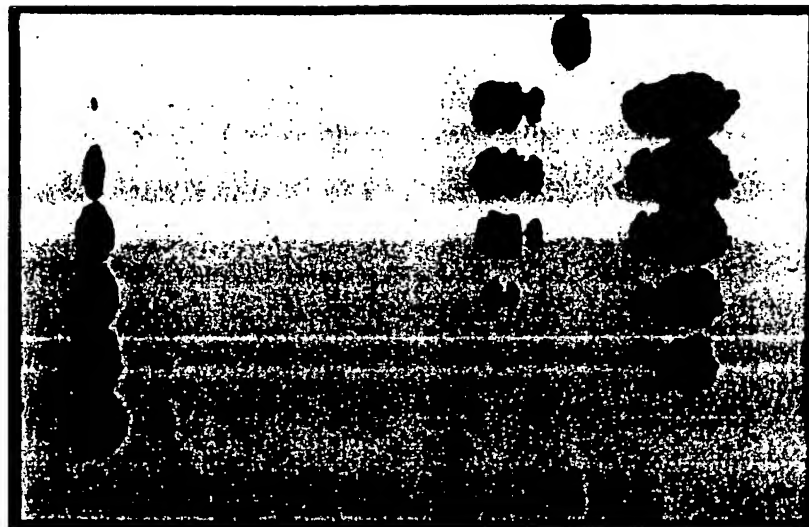


FIG. 10B

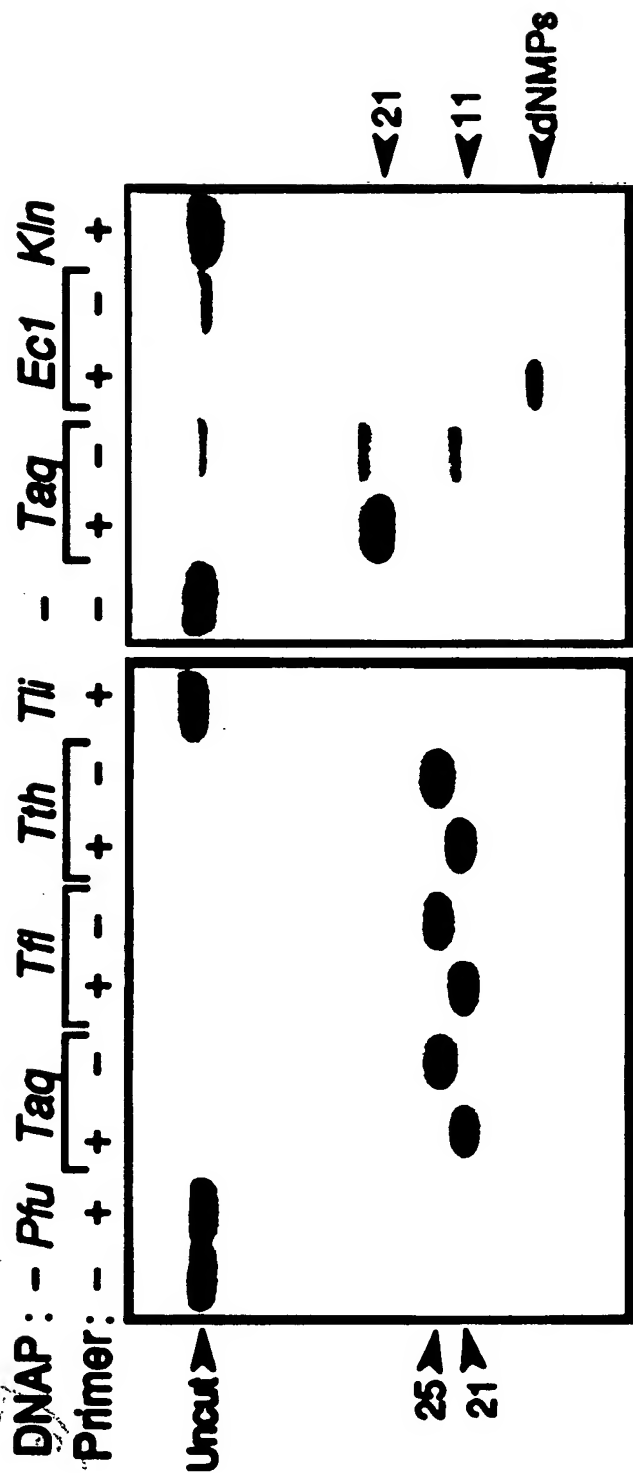


FIG. 11A

FIG. 11B

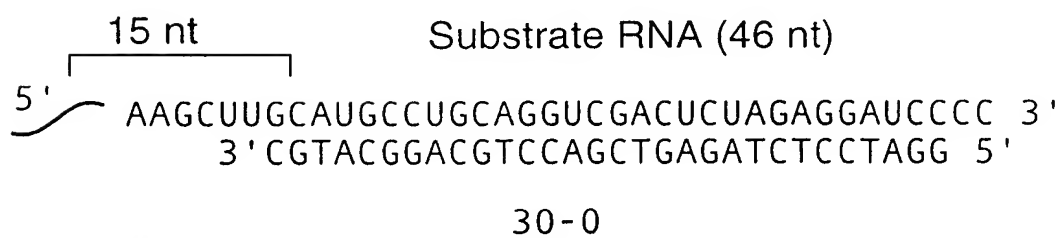
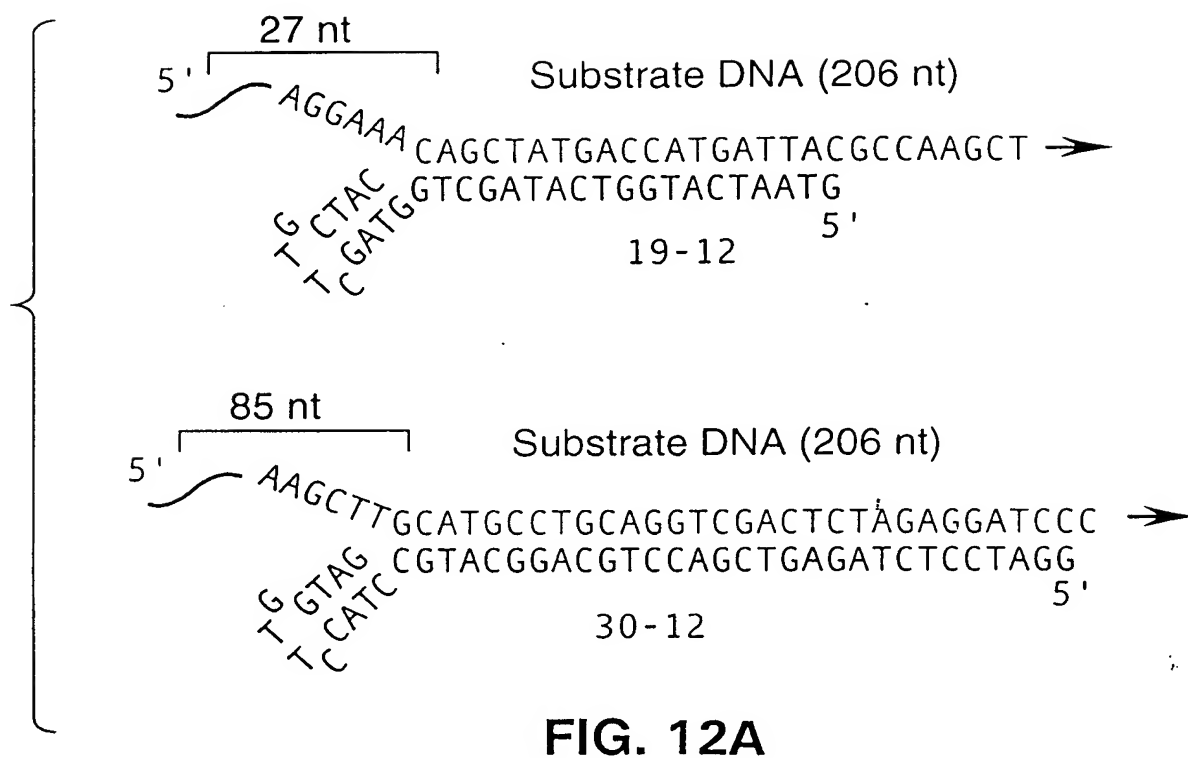


FIG. 13A

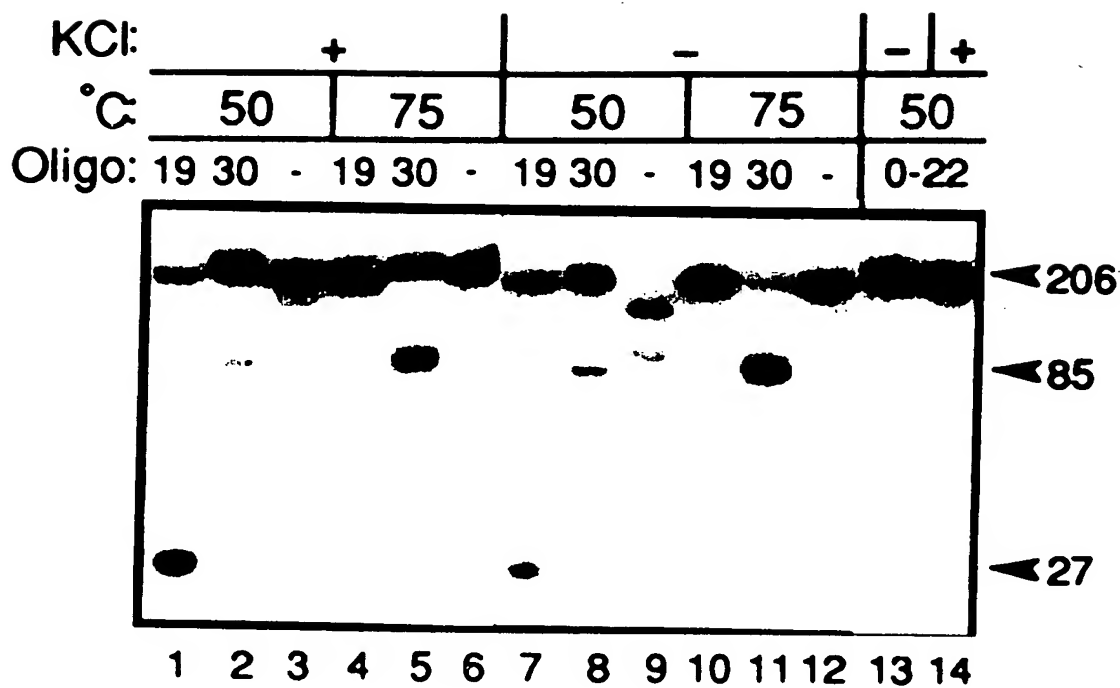


FIG. 12B

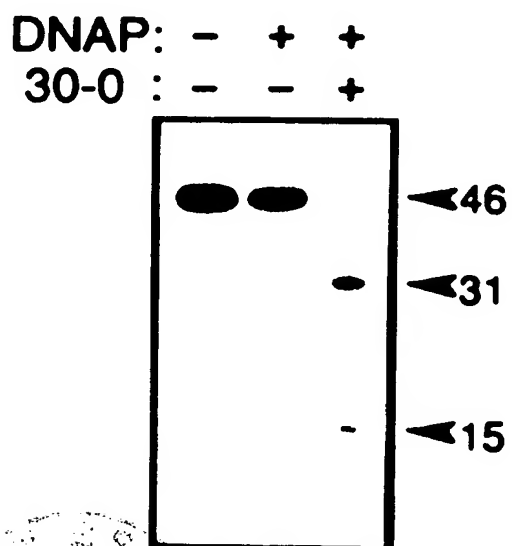


FIG. 13B

10081805-050702

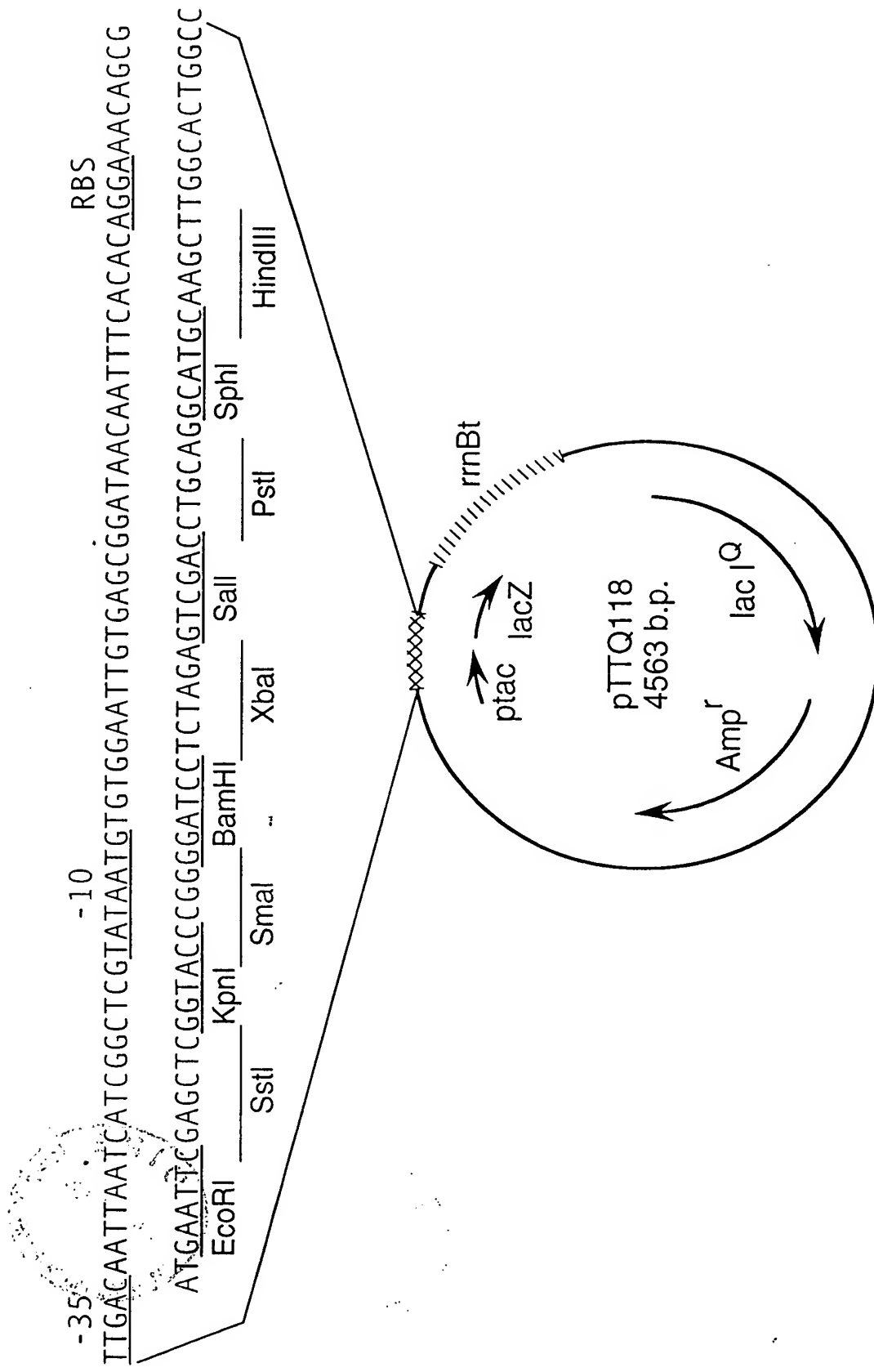
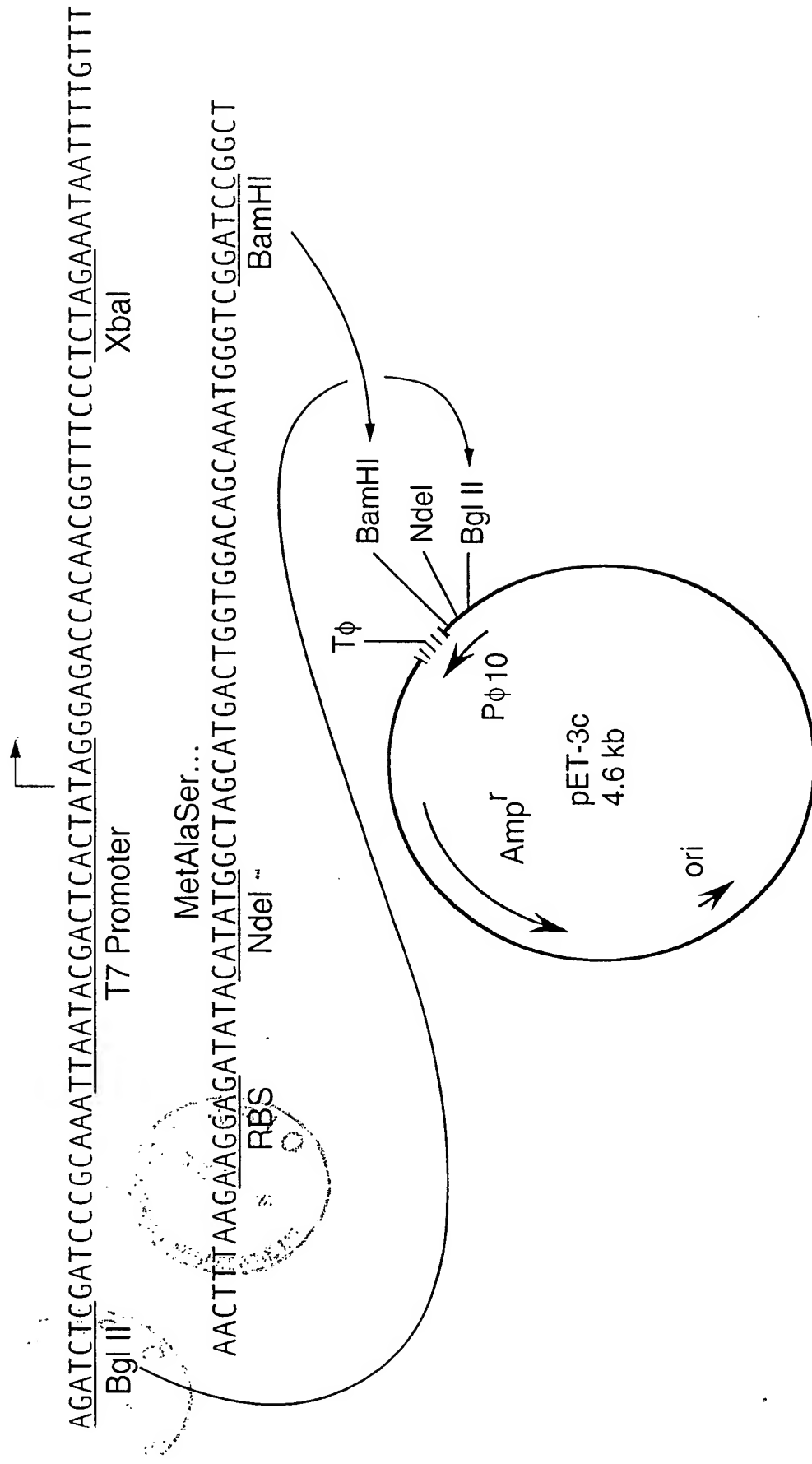


FIG. 14

205090-90819001



P ϕ 10: Bacteriophage T7 ϕ 10 promoter RBS: Ribosome binding site
T ϕ : T7 ϕ Terminator

FIG. 15

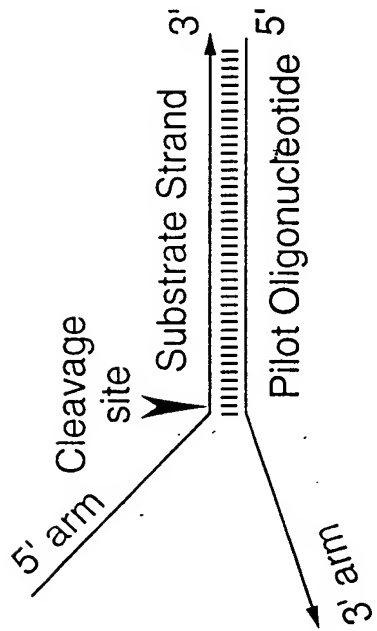


FIG. 16A

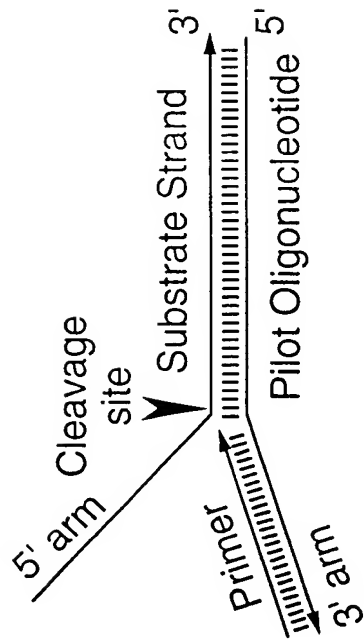


FIG. 16B

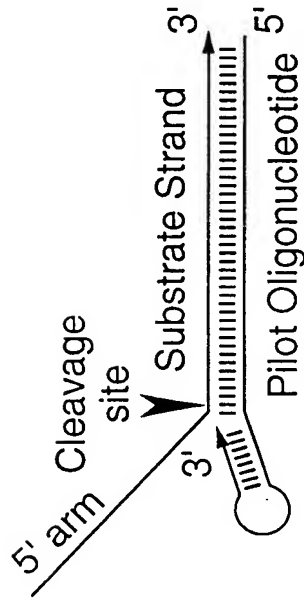


FIG. 16C

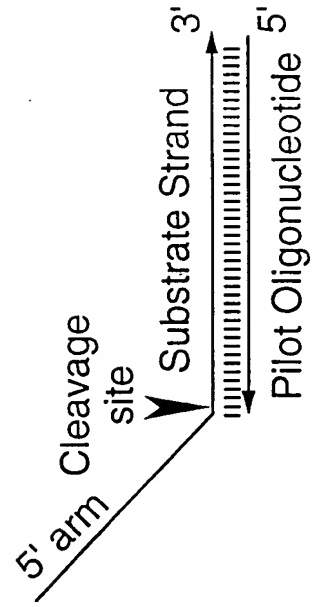


FIG. 16D

1003-1805-050702

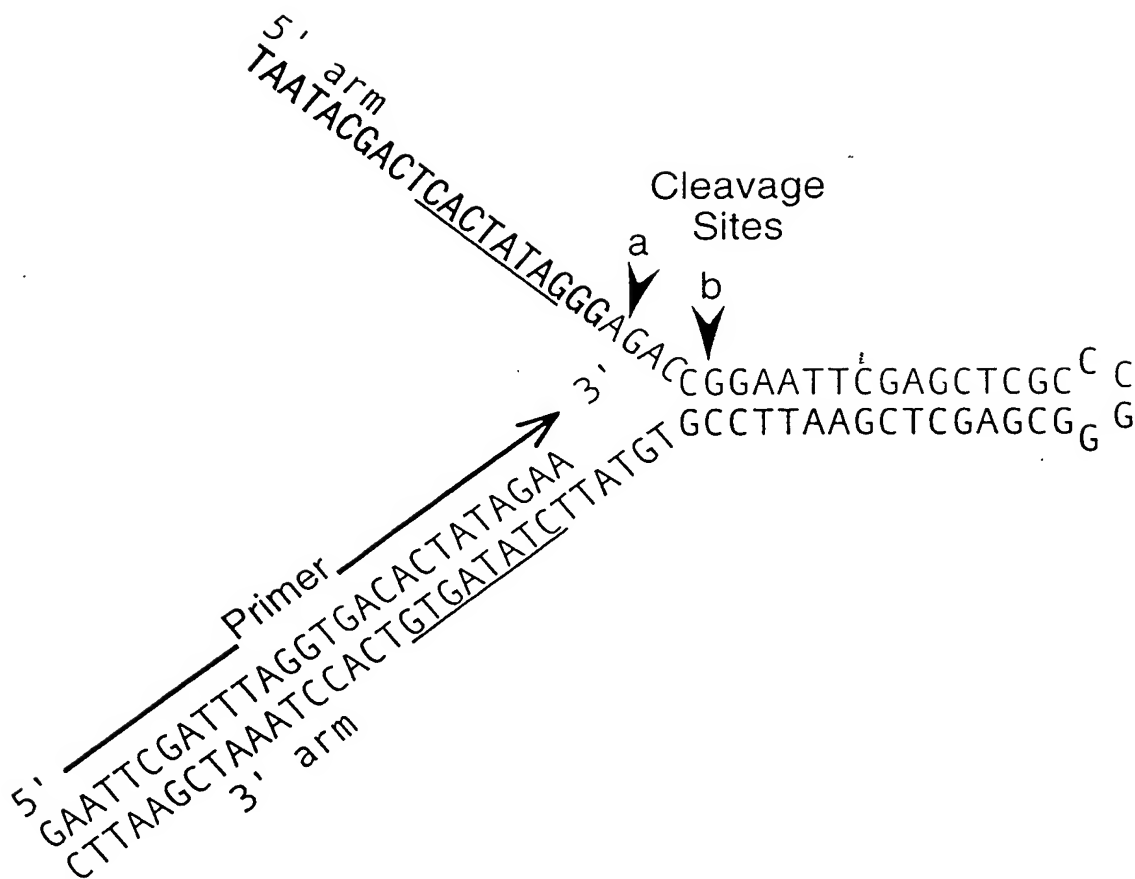


FIG. 16E

202050-90878001



1 2 3 4 5 6 7

UNCLEAVED SUBSTRATE

CLEAVED SUBSTRATE

| | | | | | | | |
|-----|----|---|---|----|---|---|--------|
| - | - | - | + | - | - | + | dNTPs |
| - | - | + | + | - | - | + | PRIMER |
| Taq | 4e | | | 5b | | | ENZYME |

FIG. 17

204090" 90818001

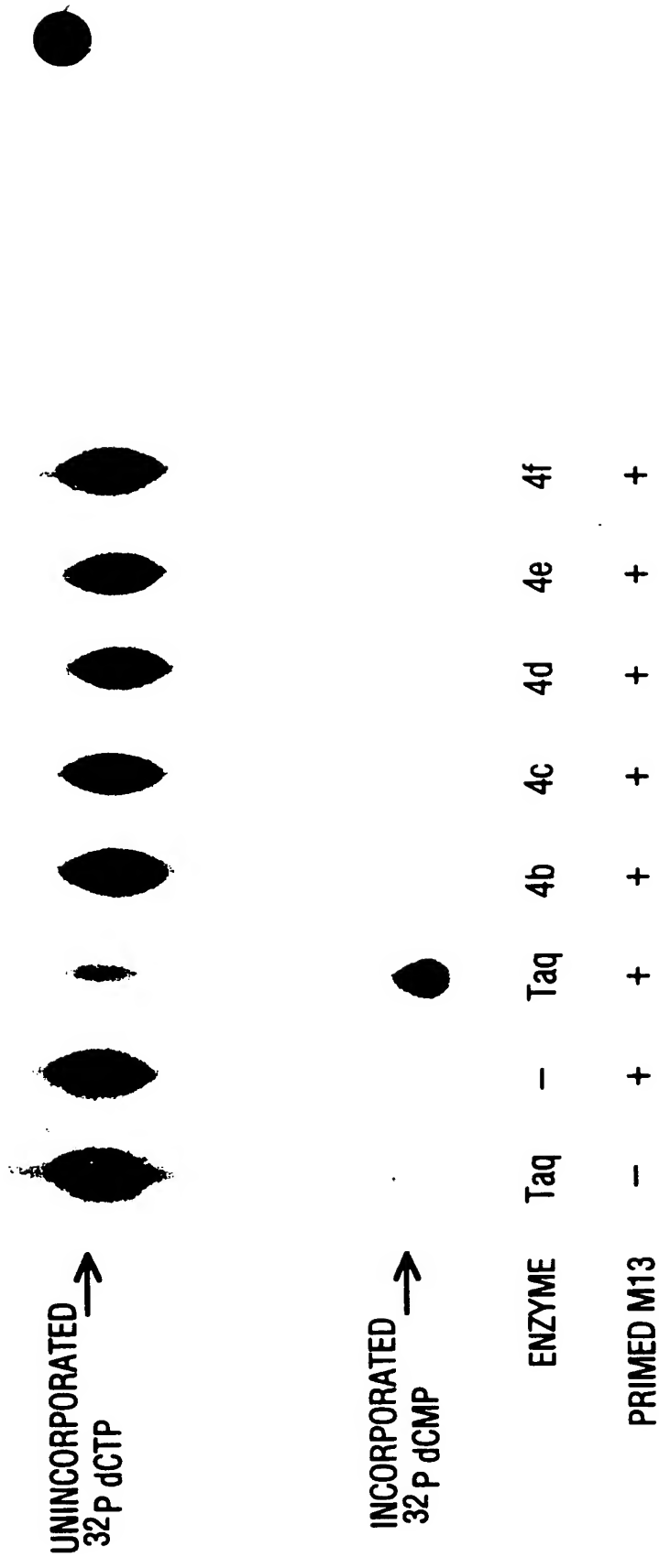


FIG. 18

10084805, 060702

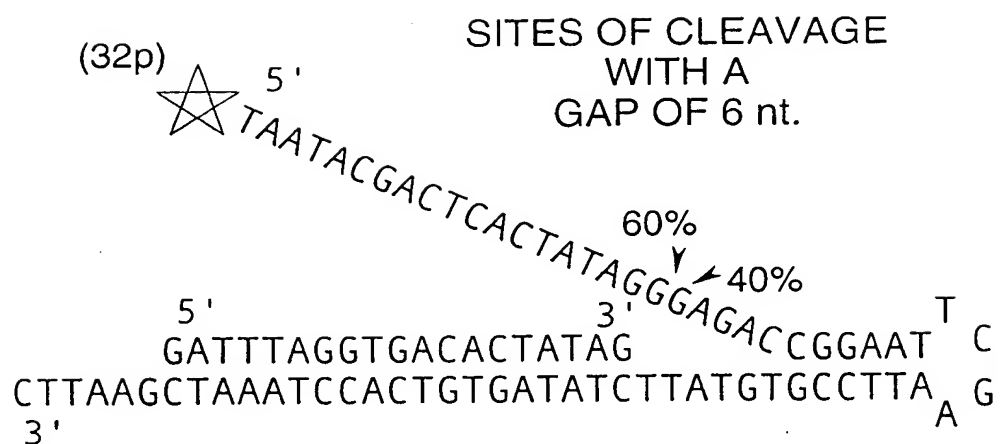


FIG. 19A



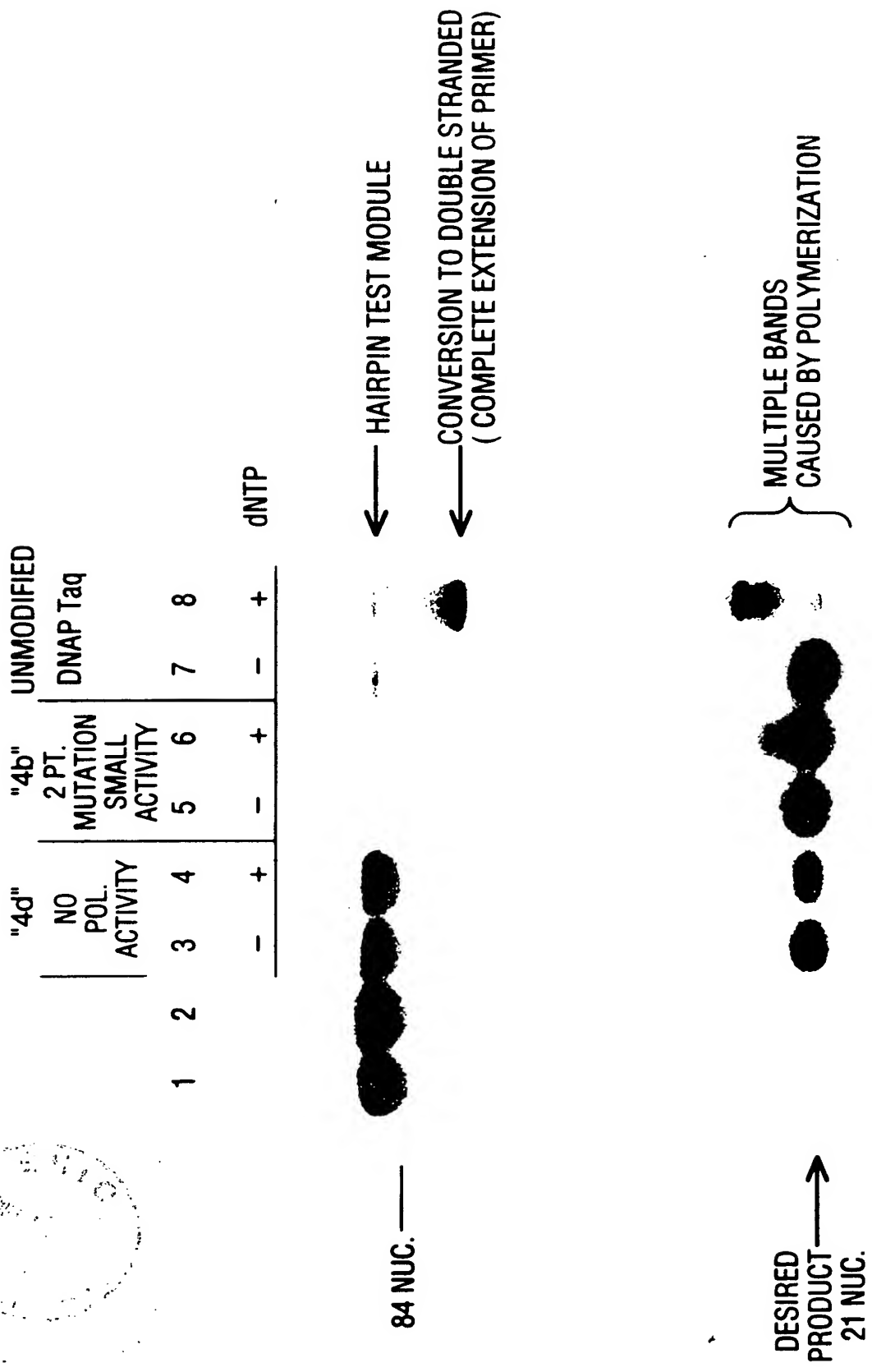


FIG. 19B

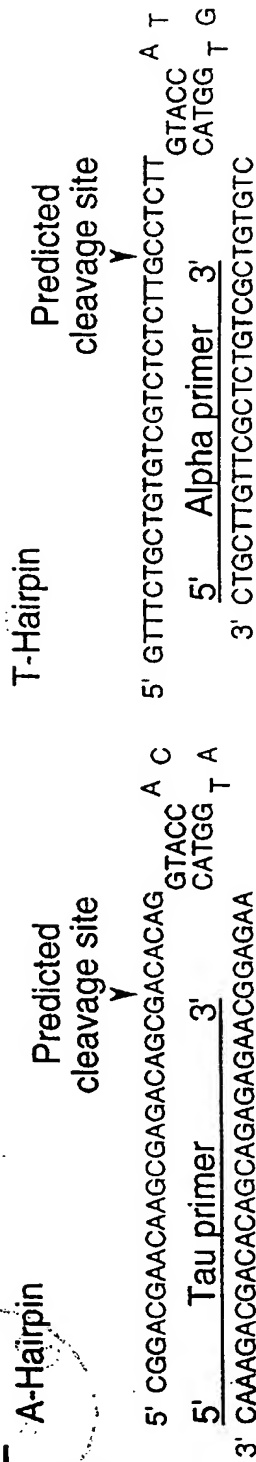


FIG. 20A

Sequence of alpha primer:
 5' GACGAAACAGCGAGACAGCG 3'

FIG. 20B

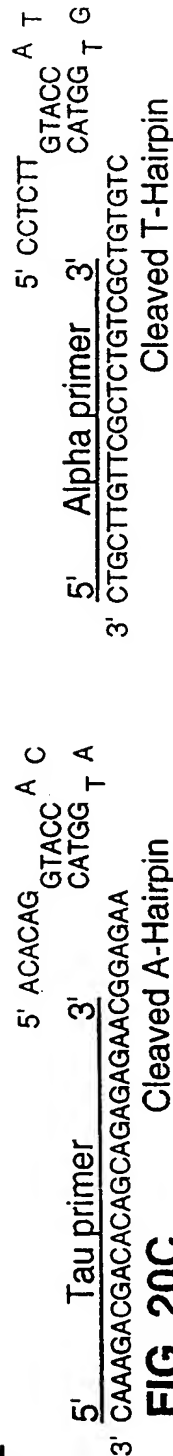


FIG. 20C

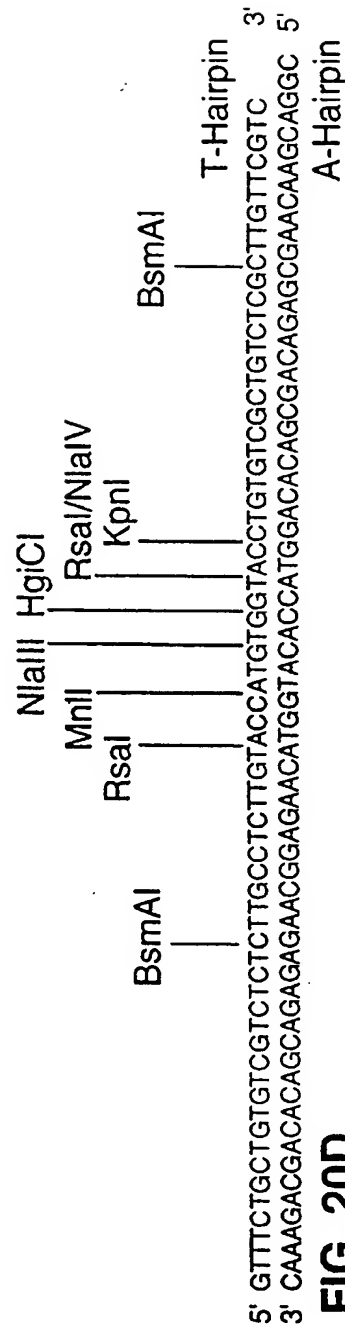


FIG. 20D

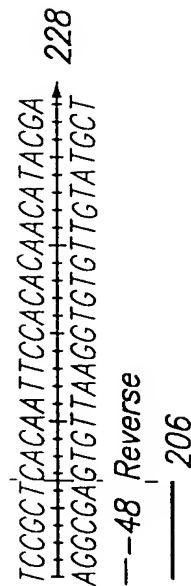
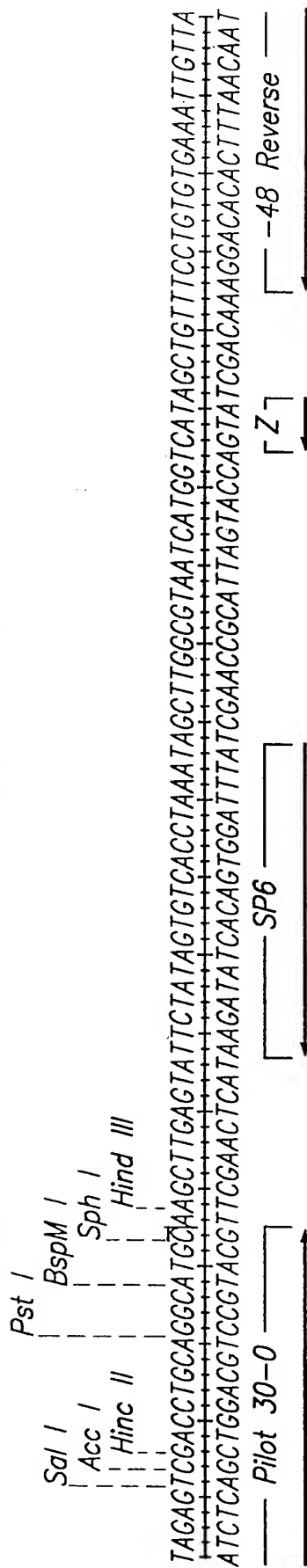
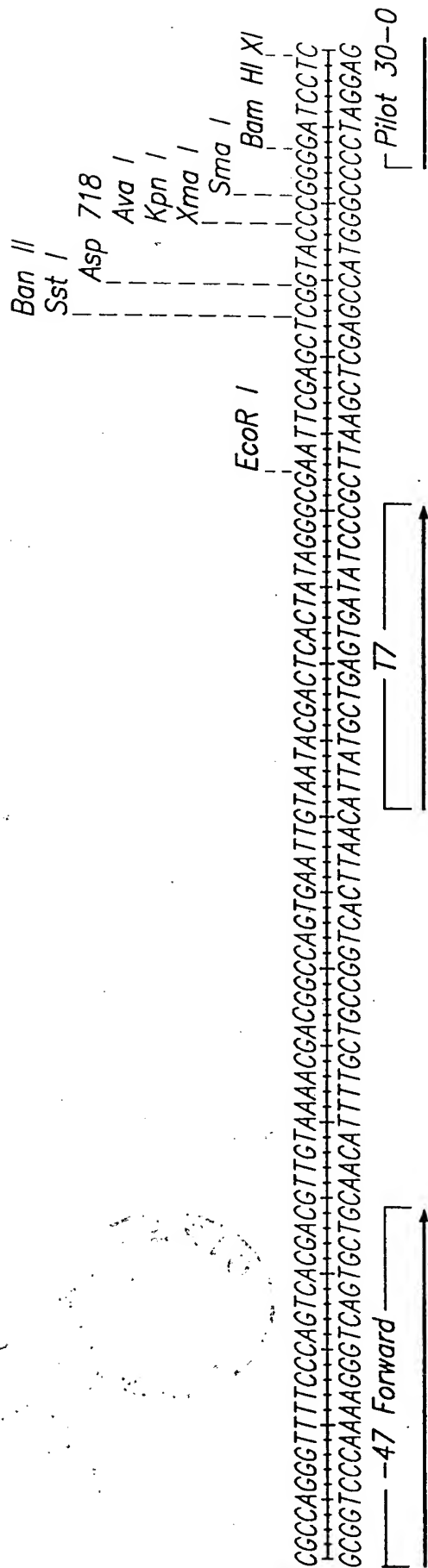


FIG. 21

10081806-060702

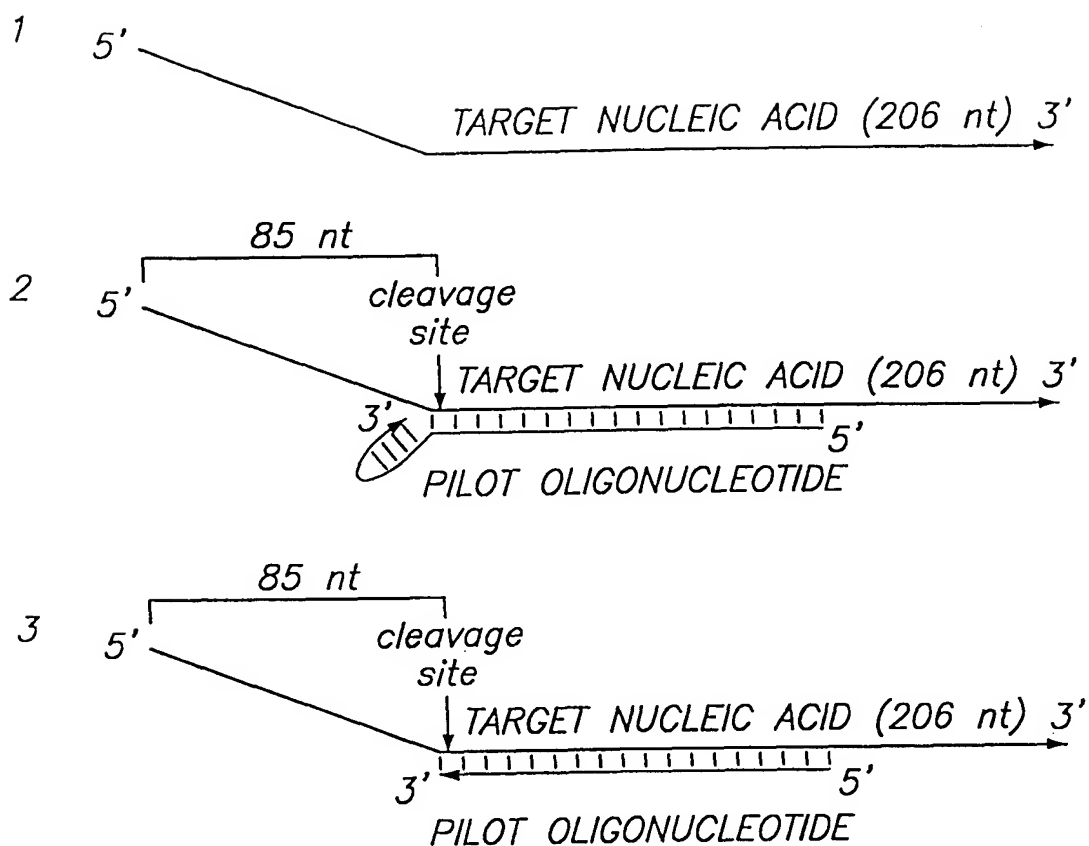


FIG. 22A



2020990" 999F999F

| I | | | II | | | III | | | IV | | | V | | | I | | | VI | | |
|---|---|---|----|---|---|-----|---|---|----|---|---|---|---|---|---|---|---|----|---|---|
| 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 |

206 —  — 206

85 —  — 85

FIG. 22B

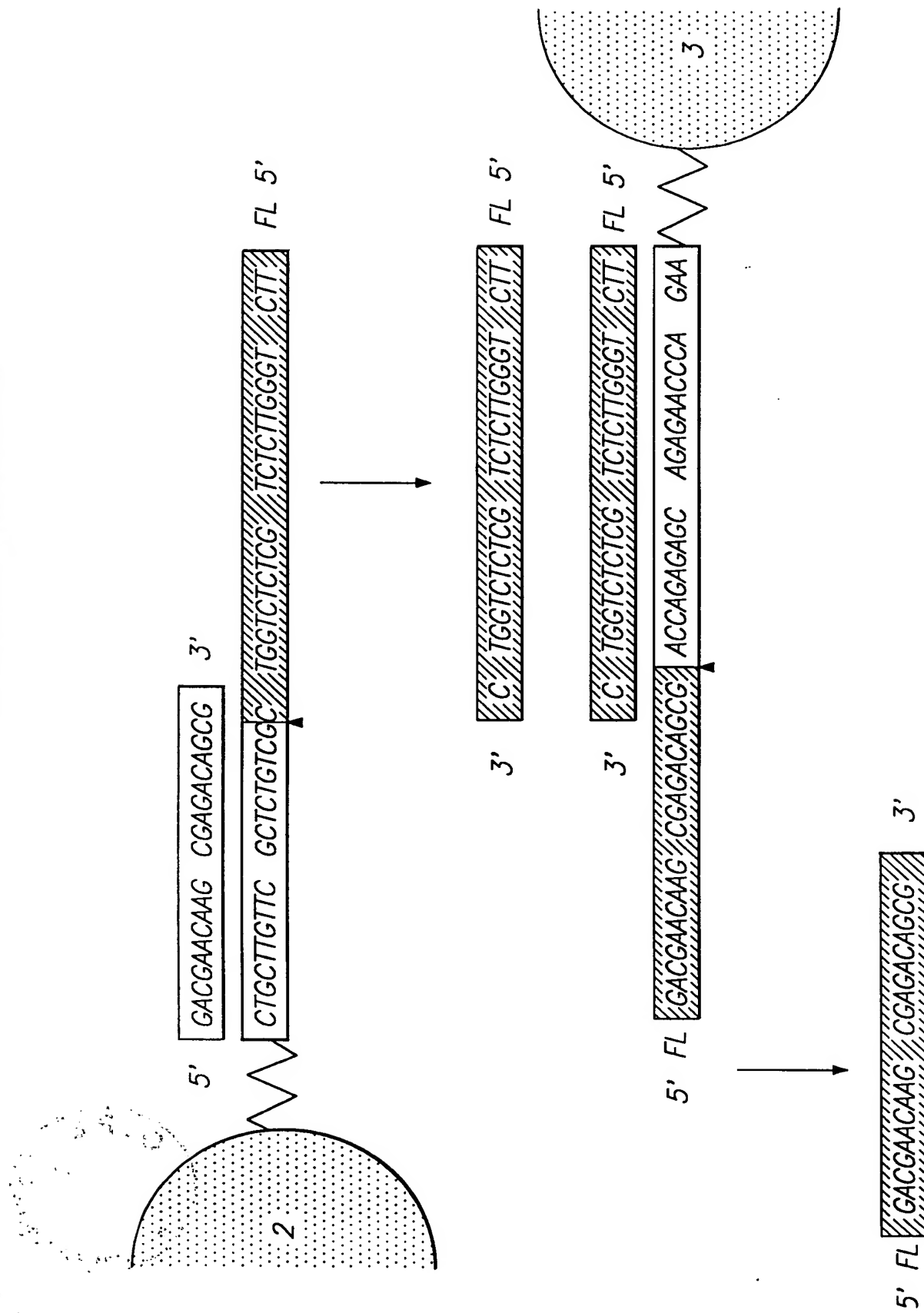
[illegible]

FIG. 23

20/090" 9081500f

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M M - + + + + - M M

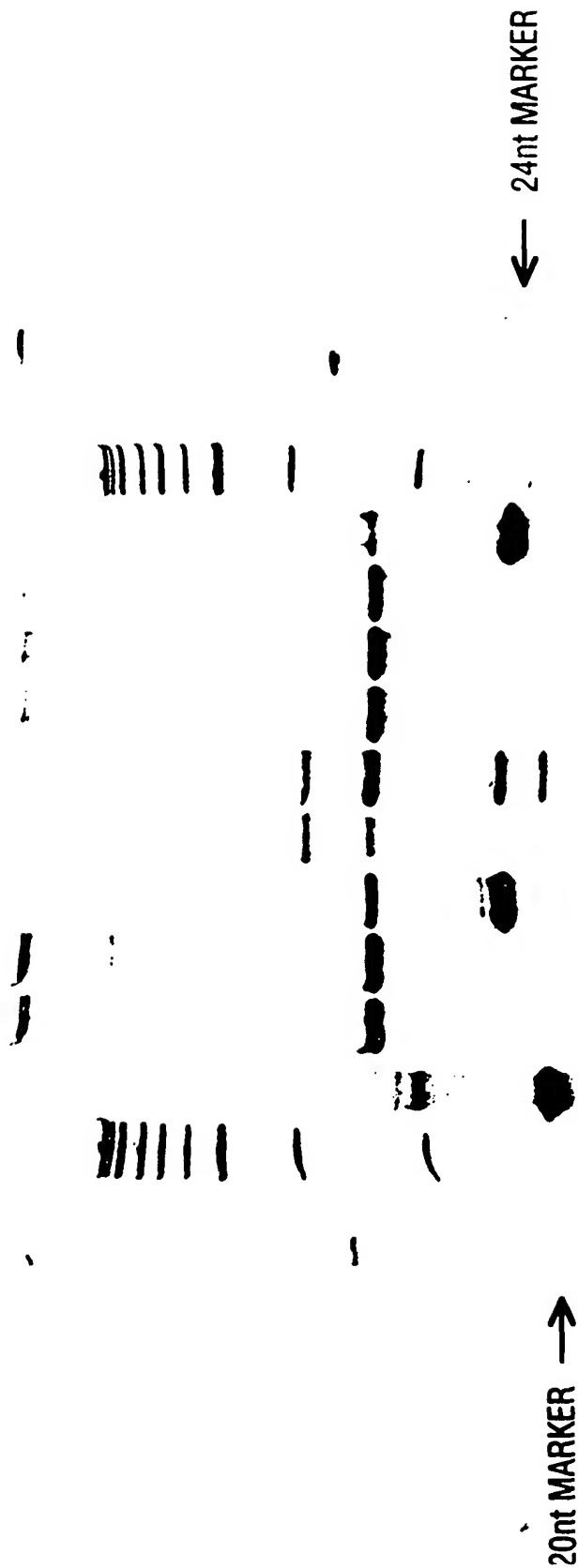


FIG. 24



204090-90818007

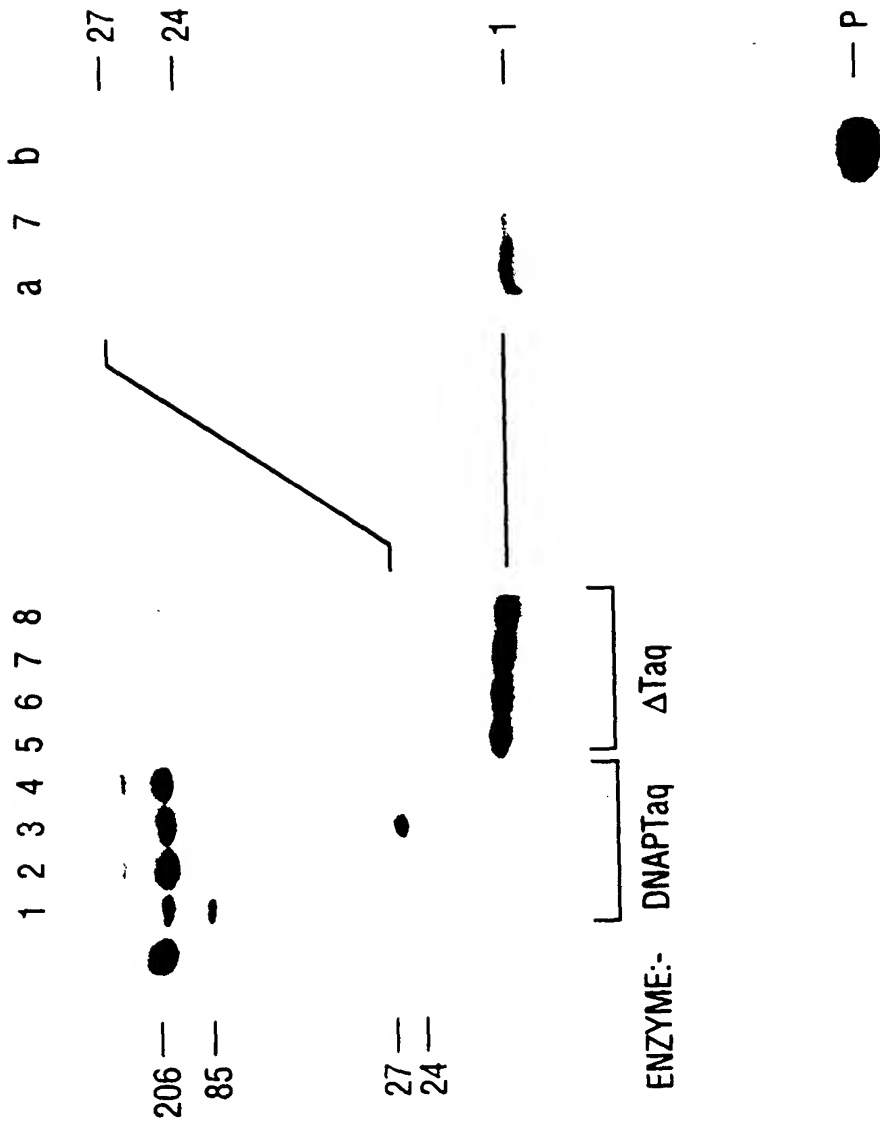


FIG. 25A FIG. 25B



2020990-90878001

FIG. 26A



FIG. 26B

* = 32p



— 206

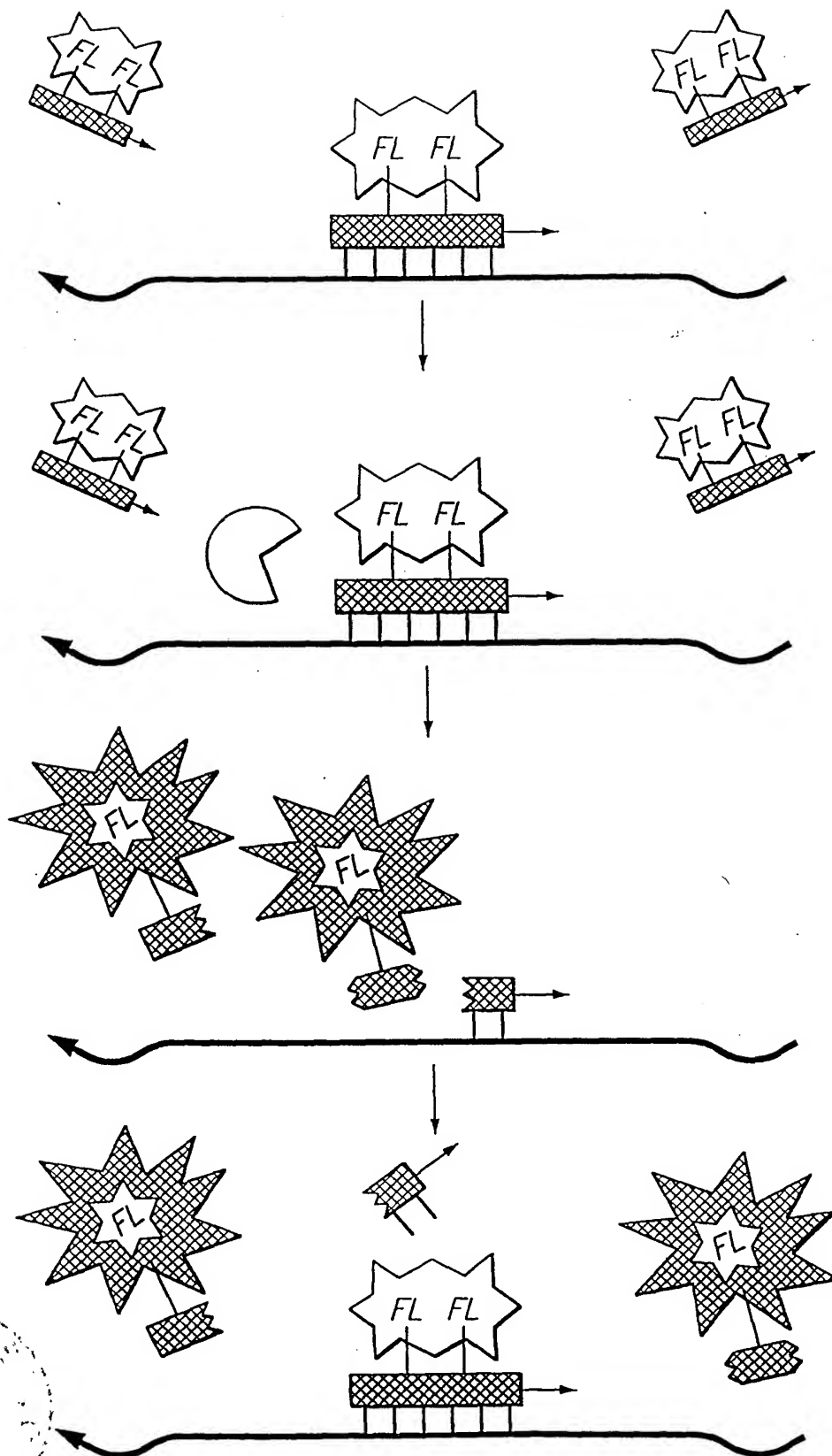


FIG. 27

10081806.060702

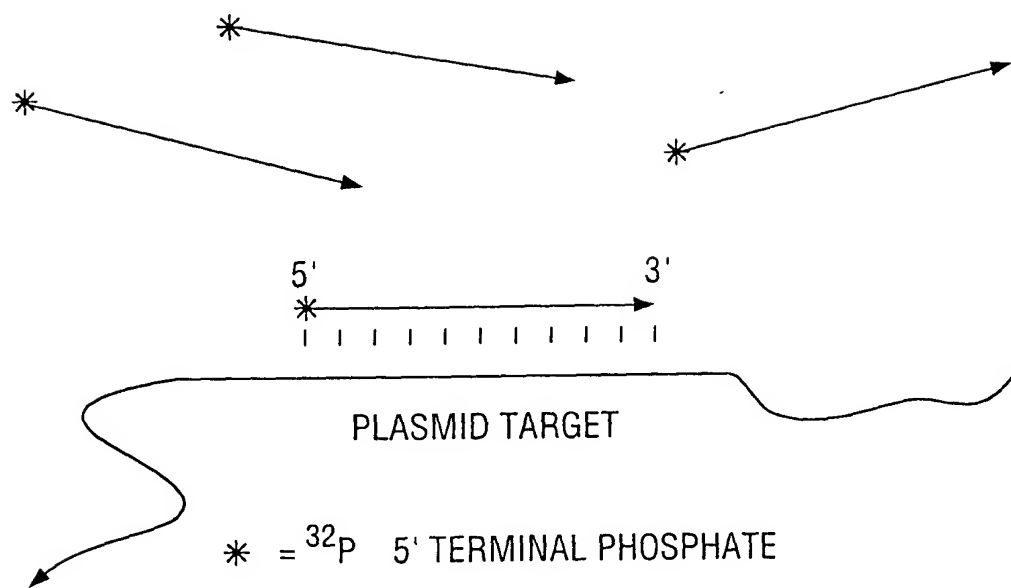


FIG. 28A



10061506.060702

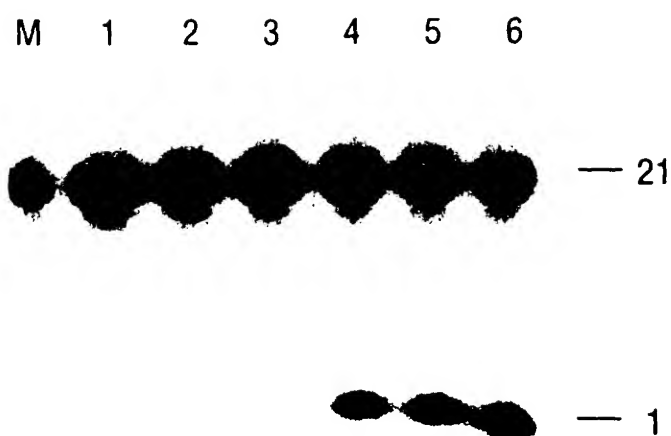
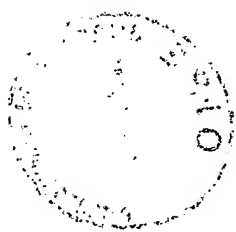


FIG. 28B



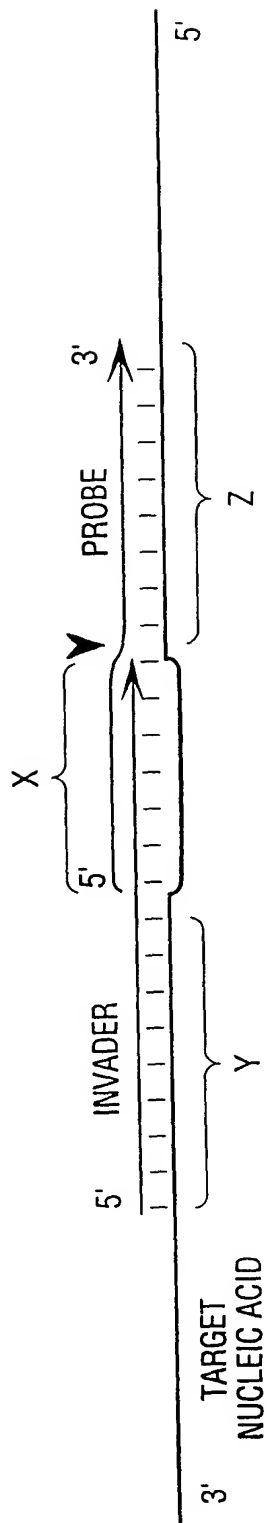
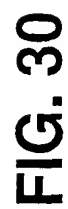


FIG. 29



10081806-050702

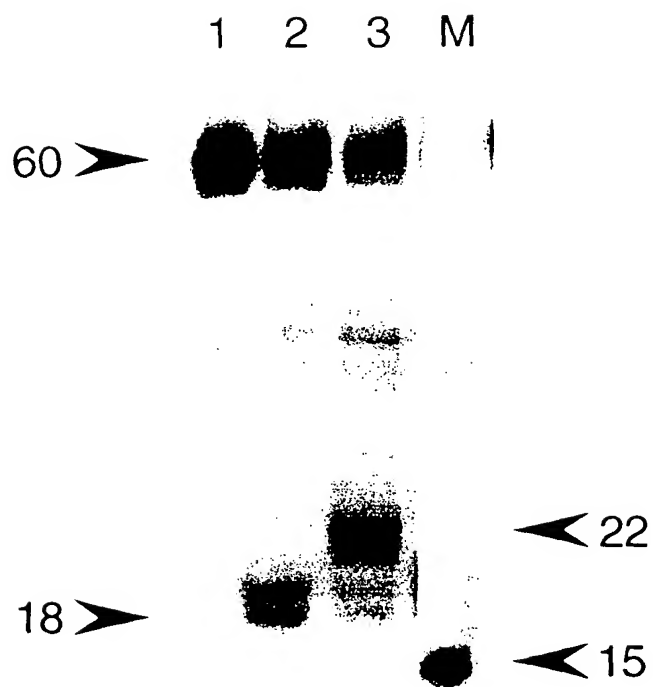


FIG. 31





204090' 90878001

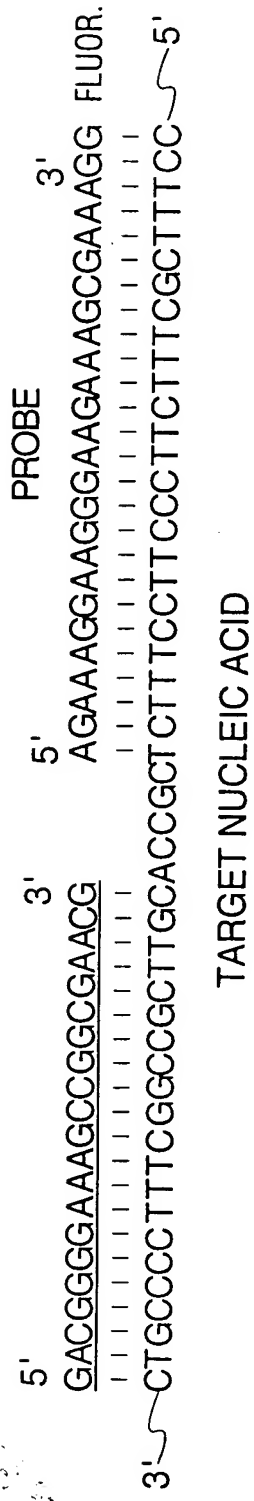


FIG. 32A

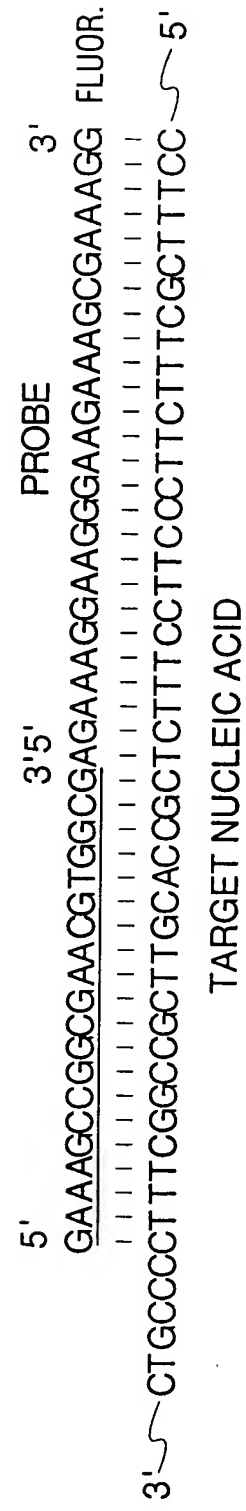


FIG. 32B

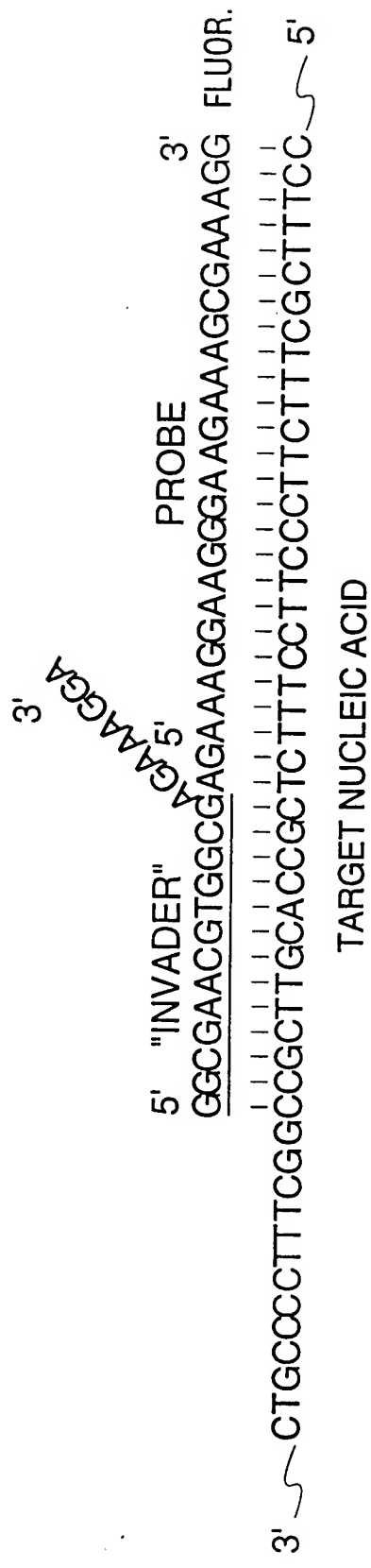
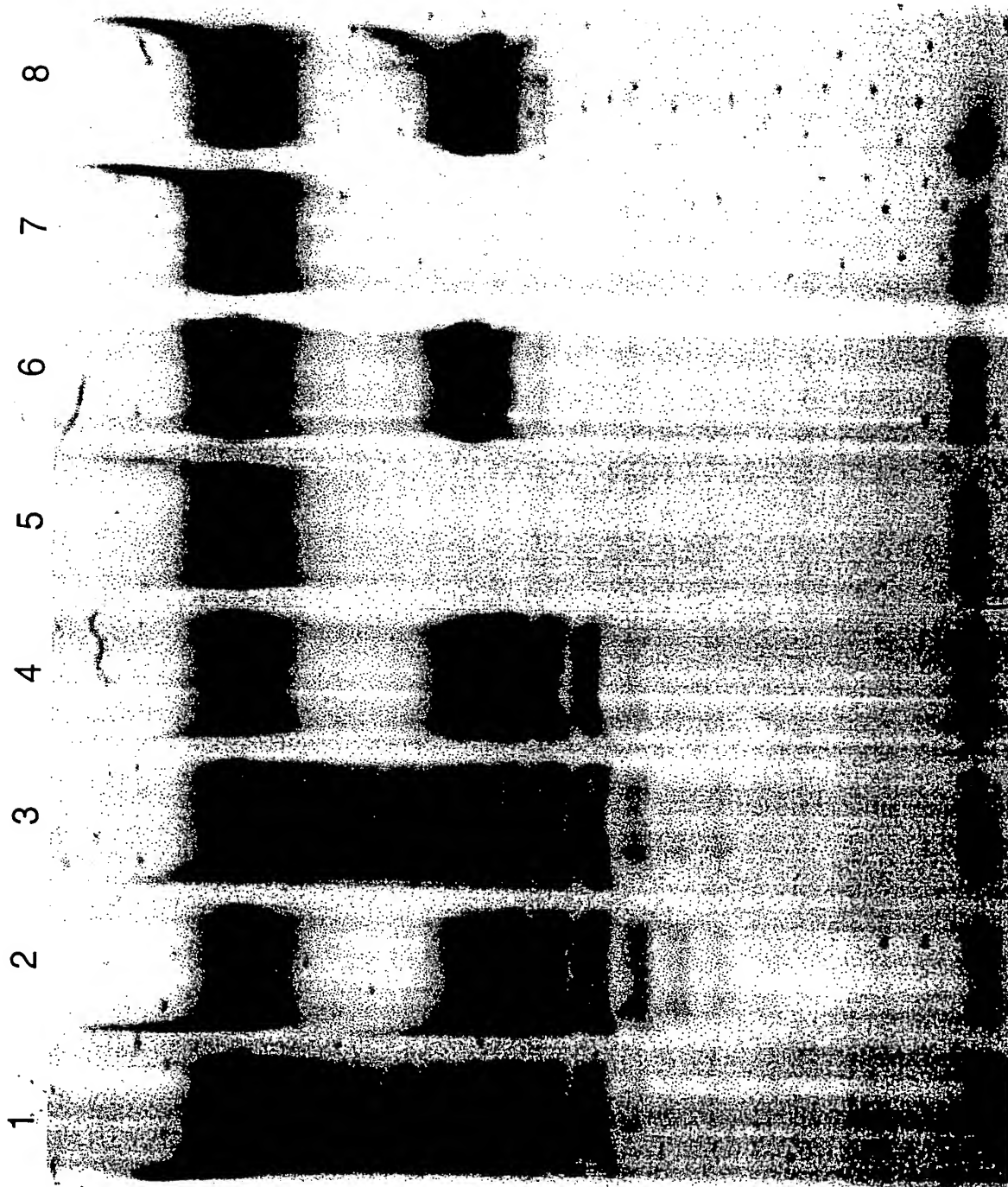


FIG. 32C

2020990-908T900f

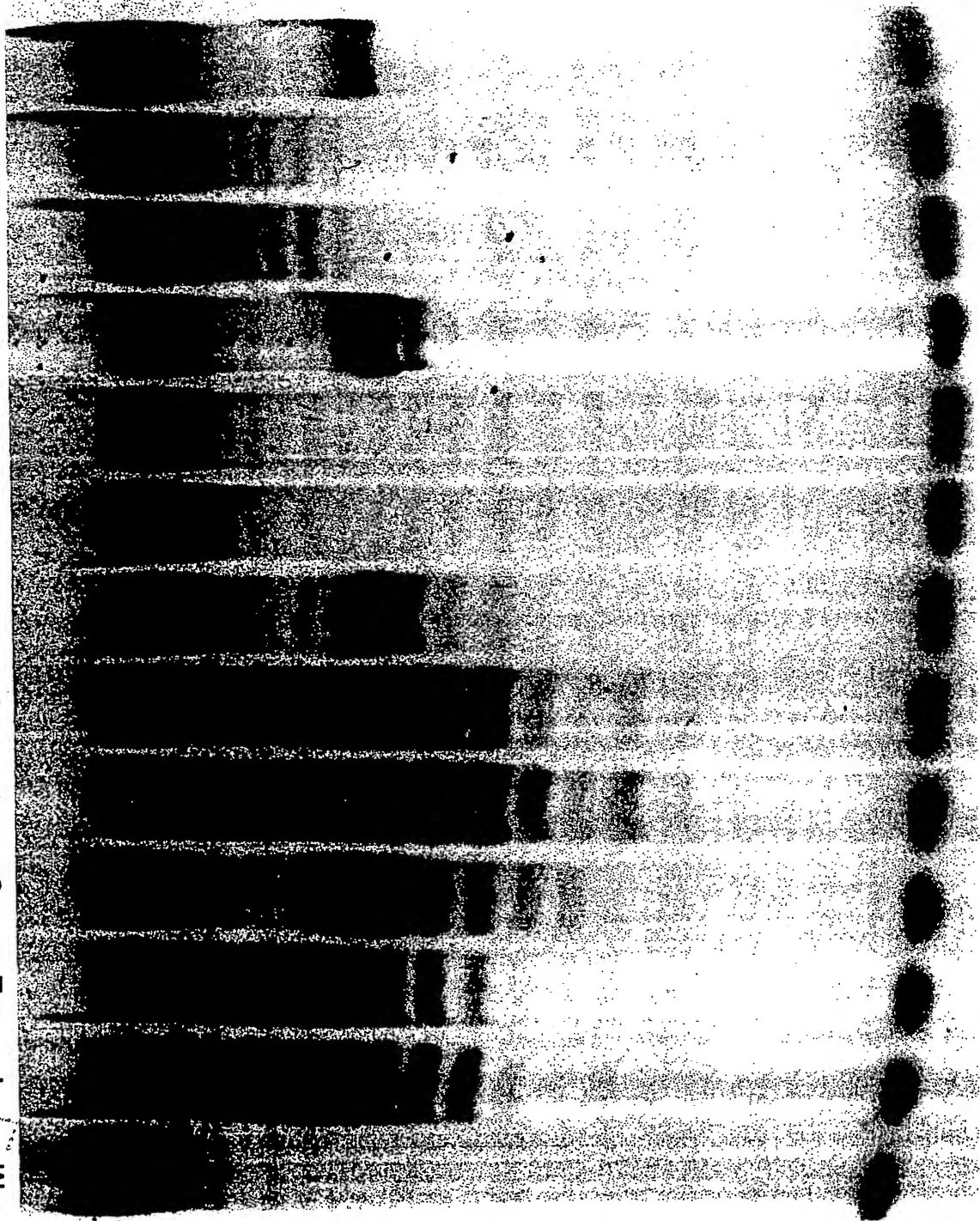


26

FIG. 33

202090" 90818001

M 1 2 3 4 5 6 7 8 9 10 11 12



26

FIG. 34

10081806.060702

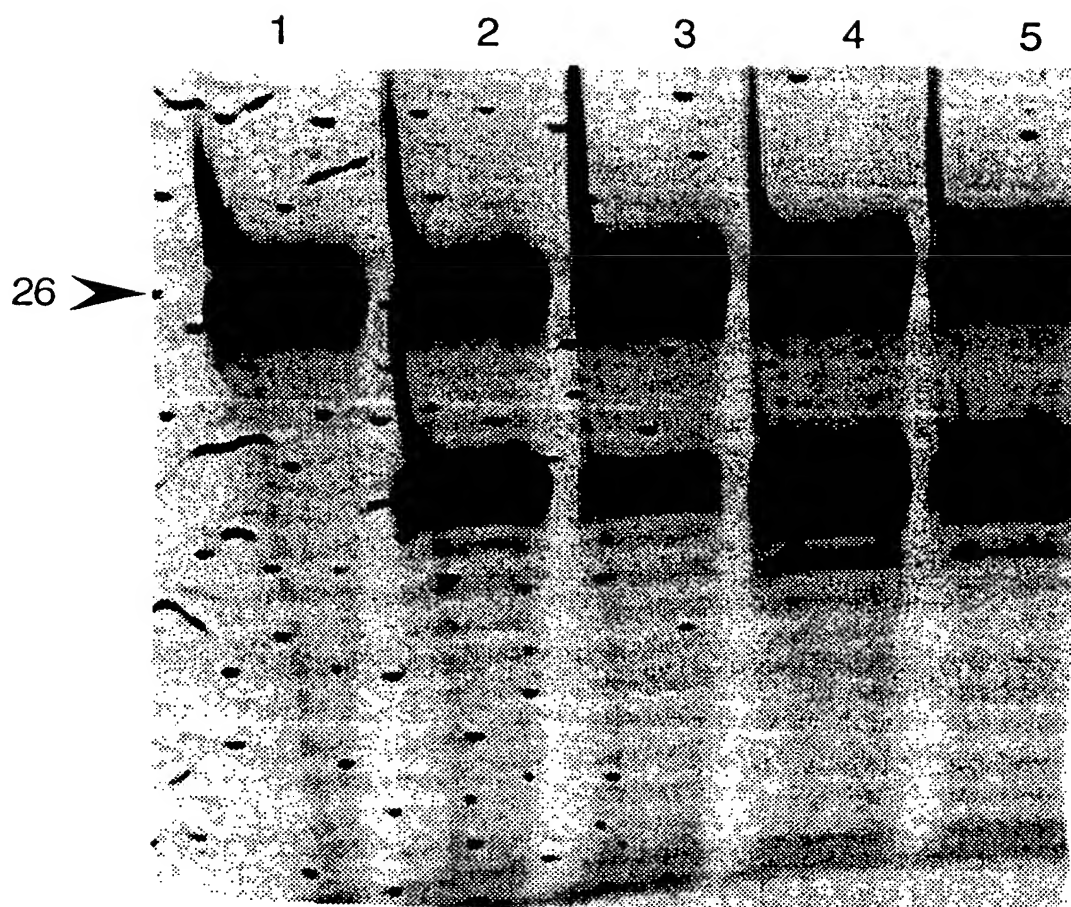
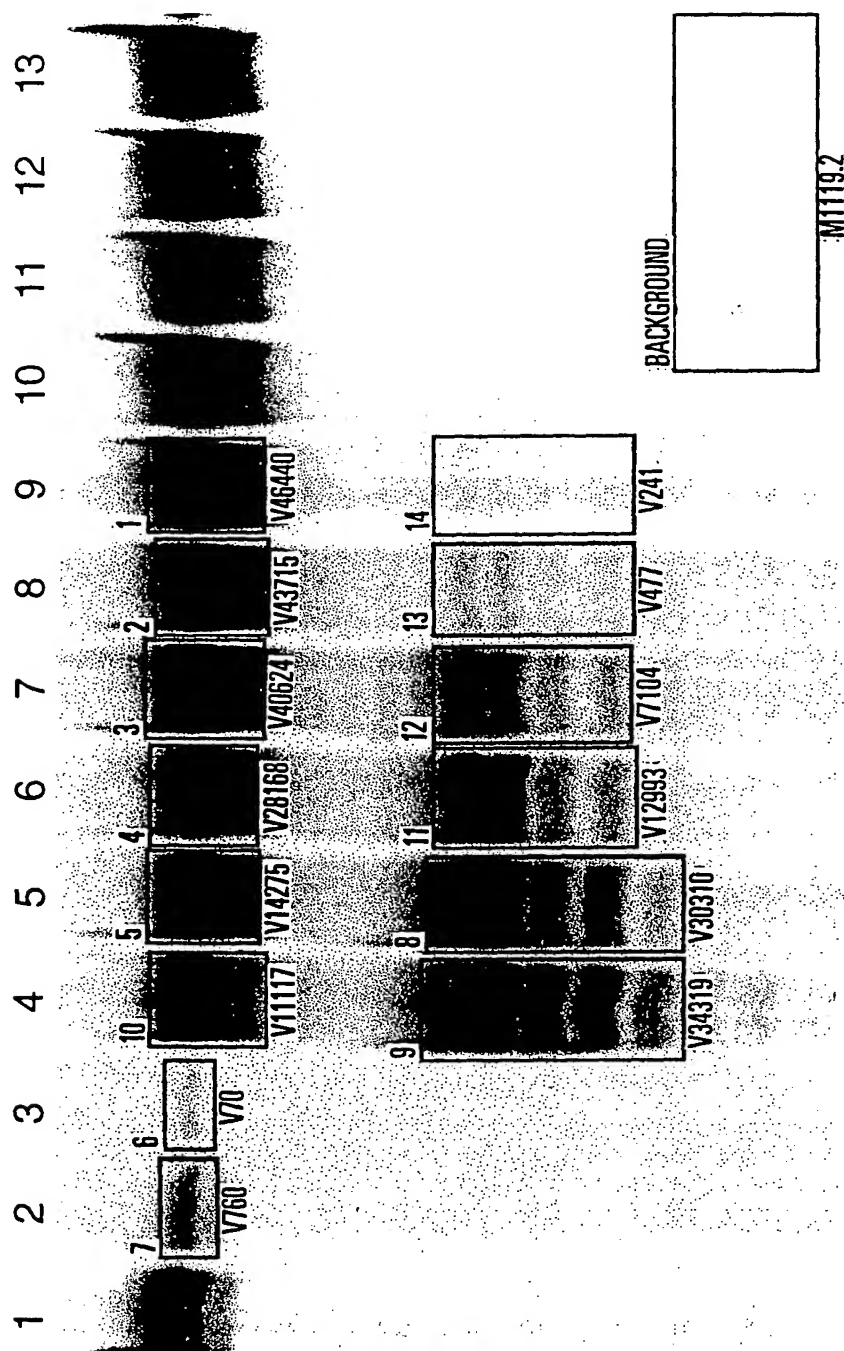



FIG. 35





202090-90878001

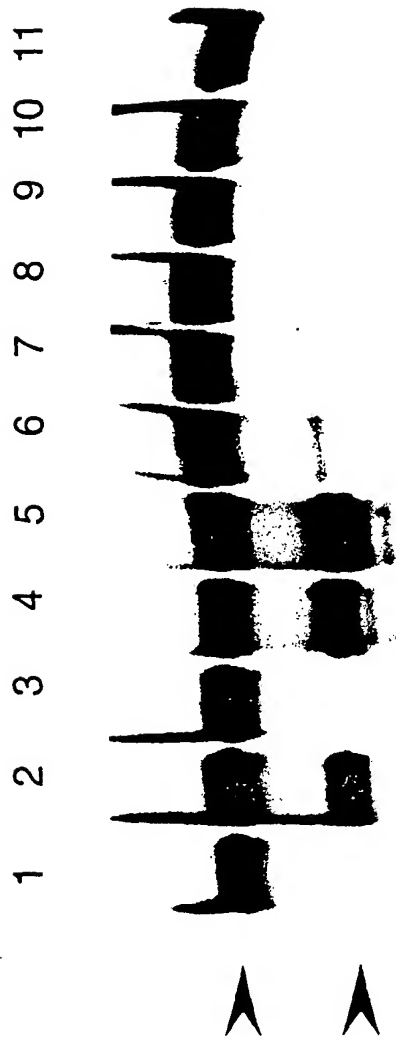


FIG. 37

20/09/2008 10:00

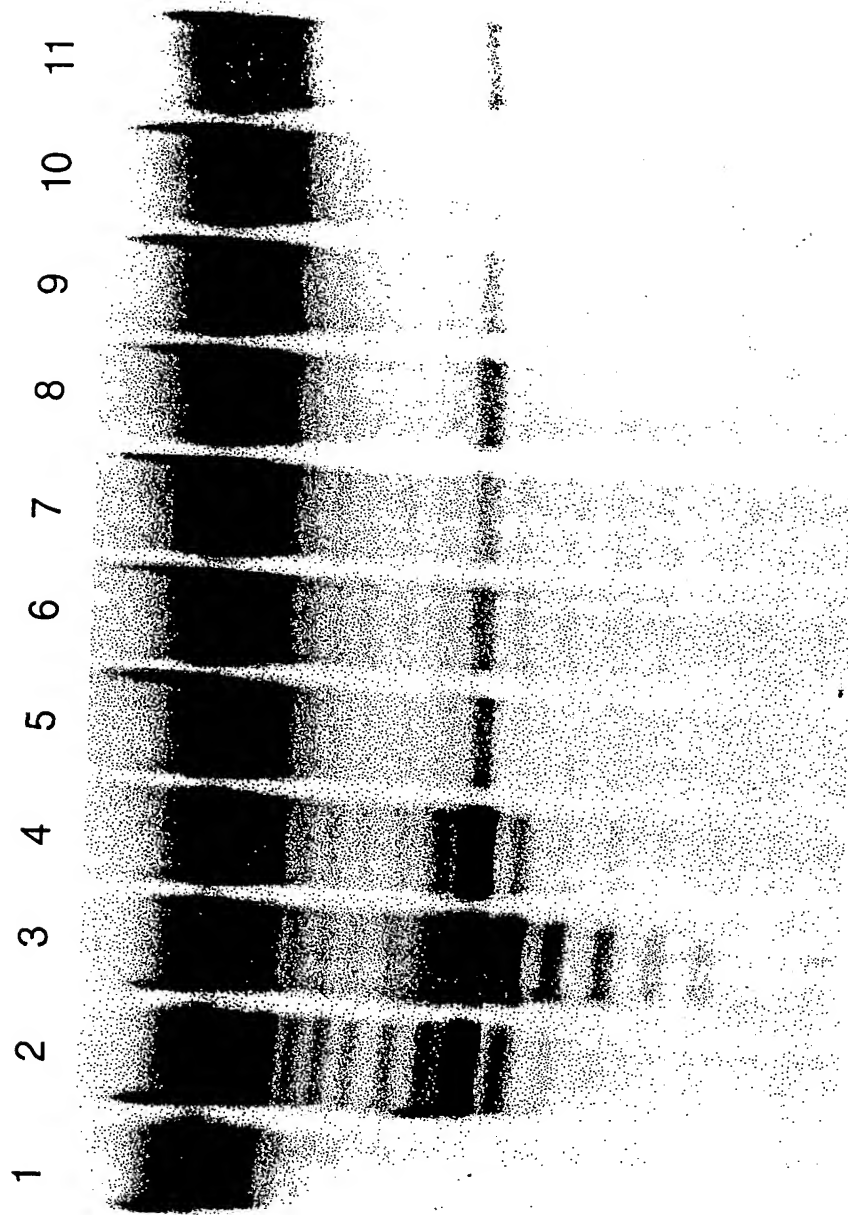


FIG. 38

10081806 050709

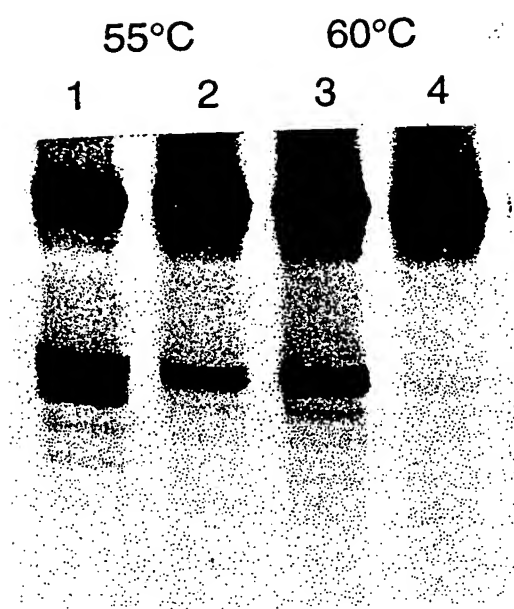


FIG. 39



10081805.060702

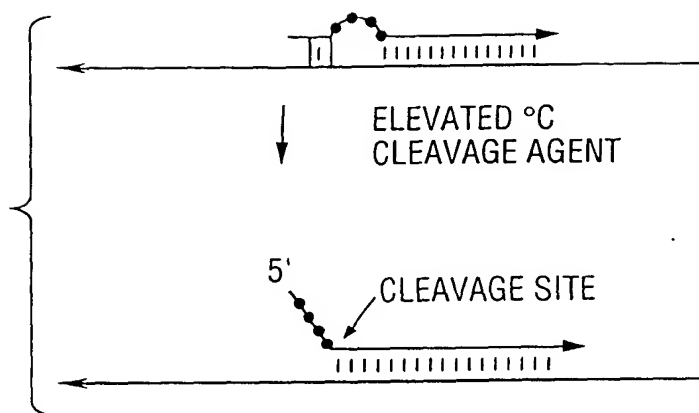


FIG. 40A

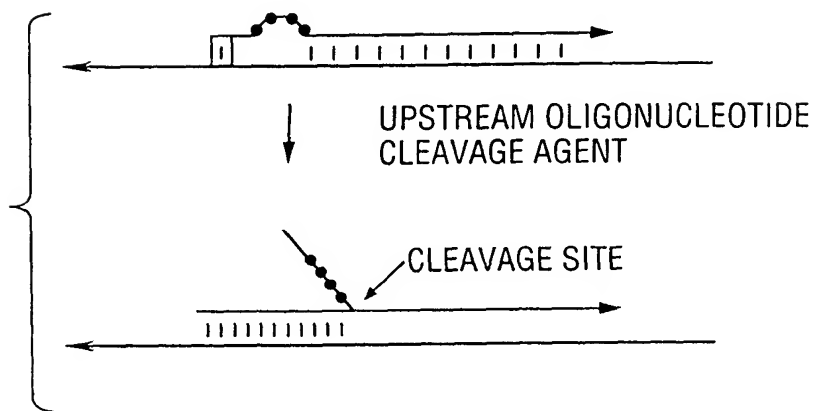


FIG. 40B

20/09/99 09:59:00

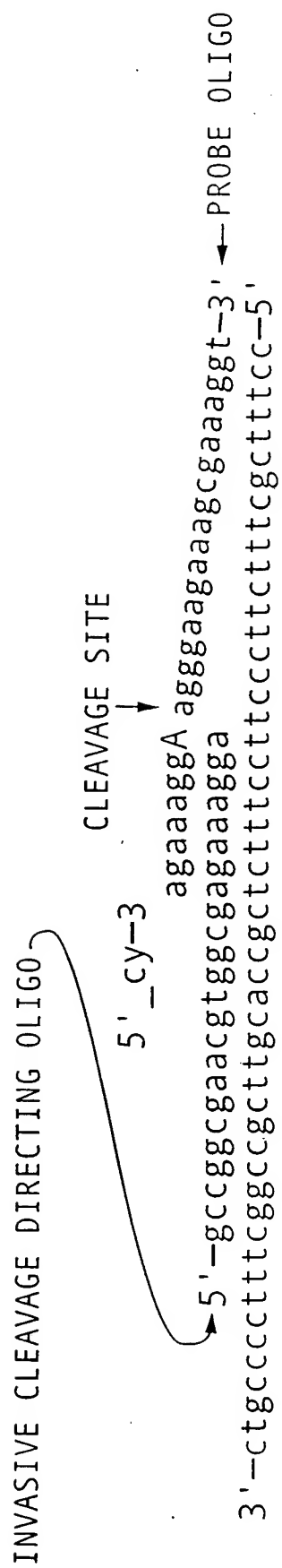


FIG. 41

10081806.060702

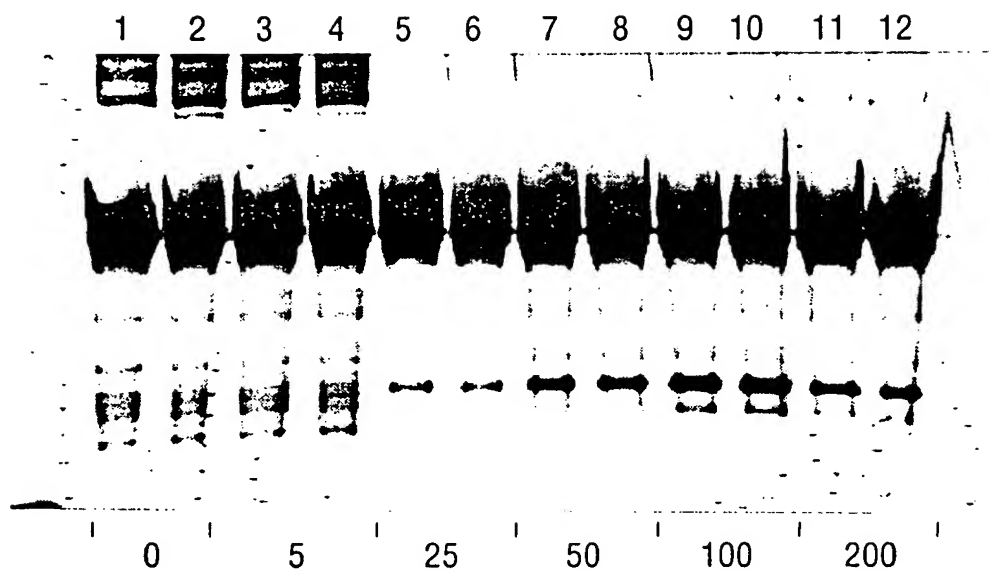
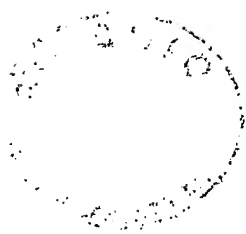


FIG. 42



10031806.060702

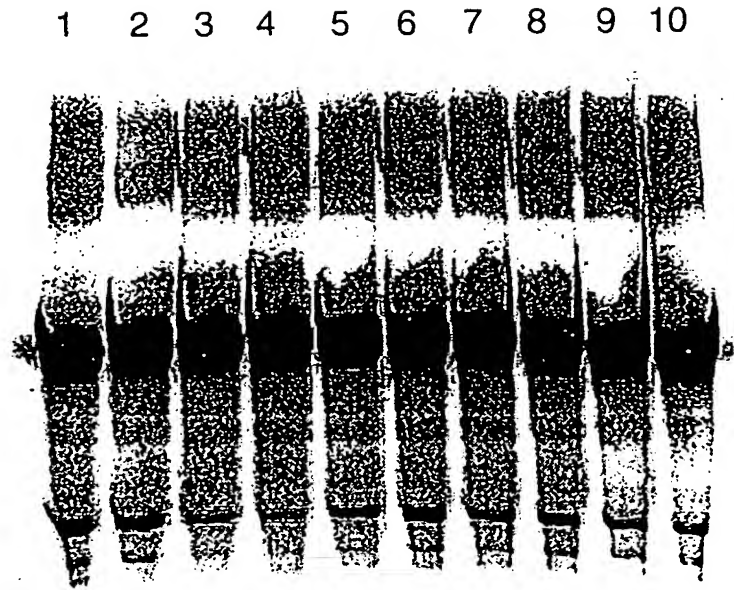
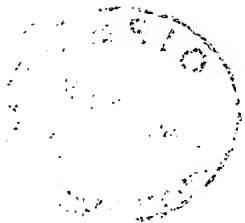


FIG. 43



10081806-060702

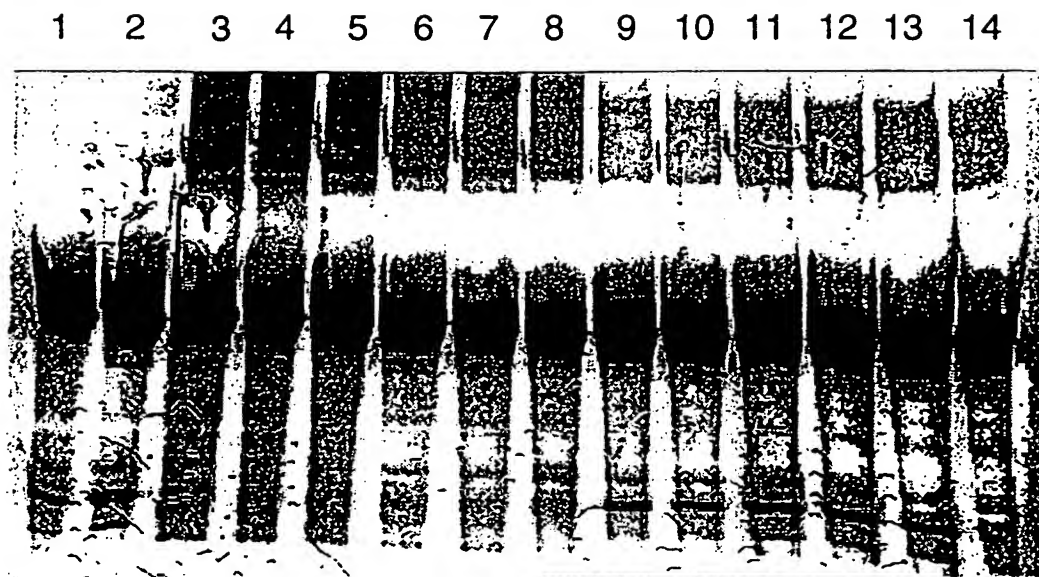


FIG. 44



202090" 90819001

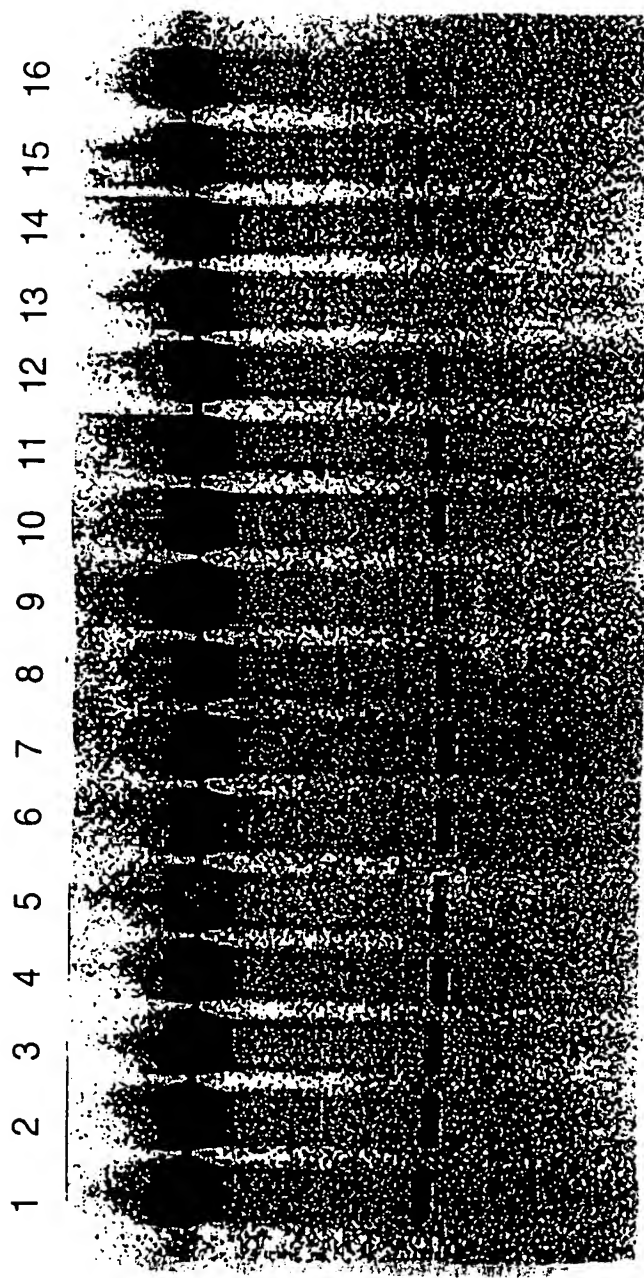


FIG. 45

10081805-060702

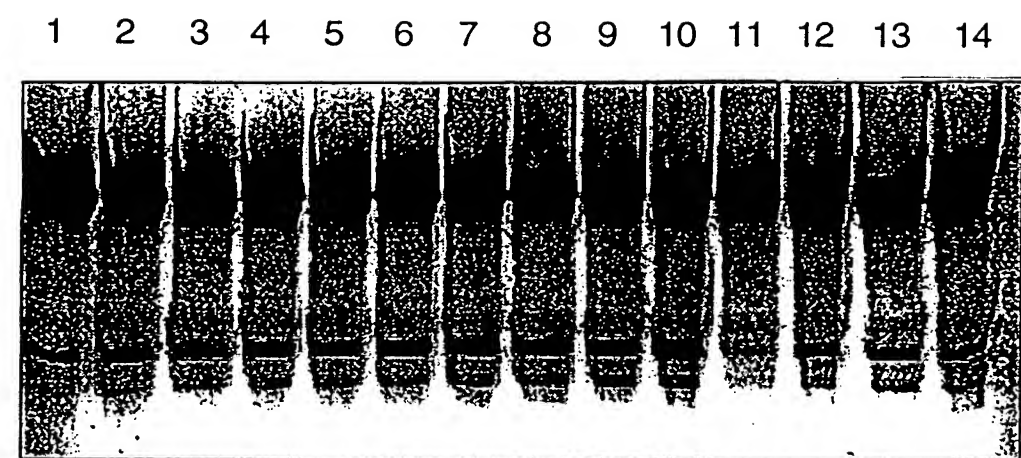


FIG. 46



10081806.060702

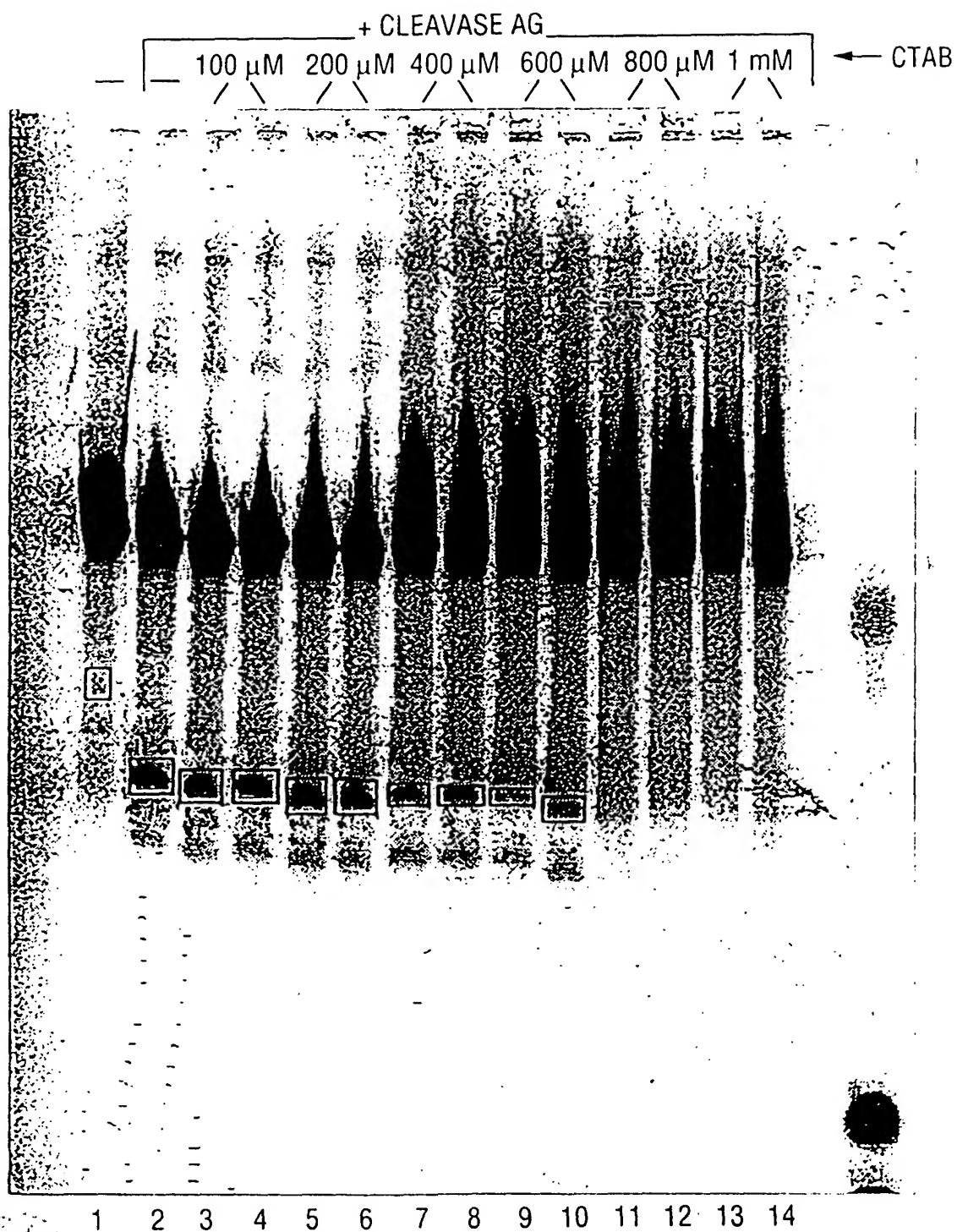


FIG. 47

10081506.060702

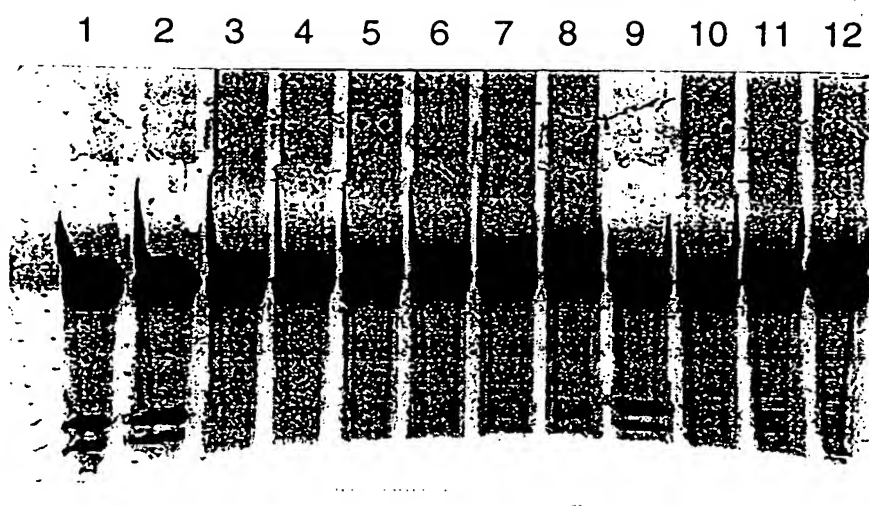


FIG. 48

10081806.050702
204090-90878001

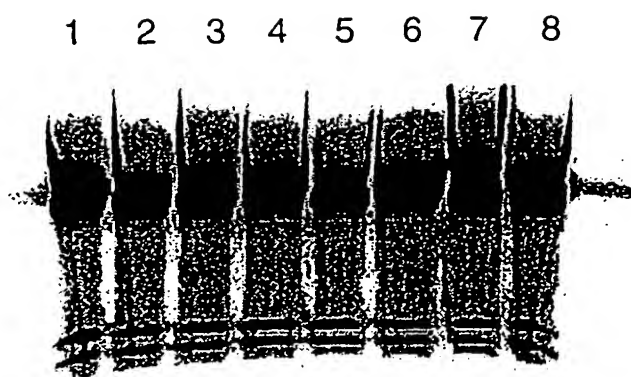


FIG. 49



10081806 . 060702

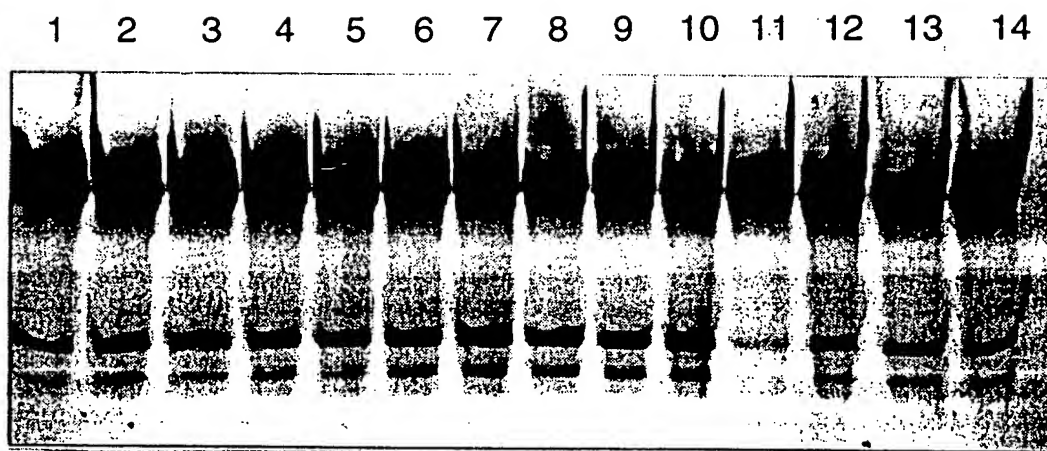


FIG. 50

10081805.060702

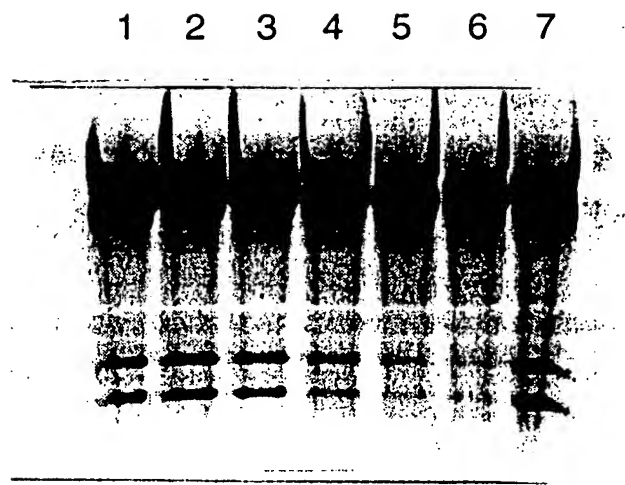


FIG. 51



10081806-060702

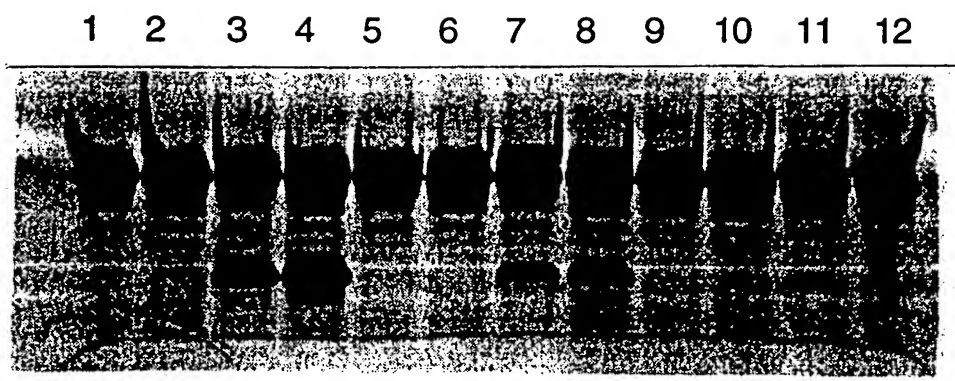


FIG. 52



202090-90818001

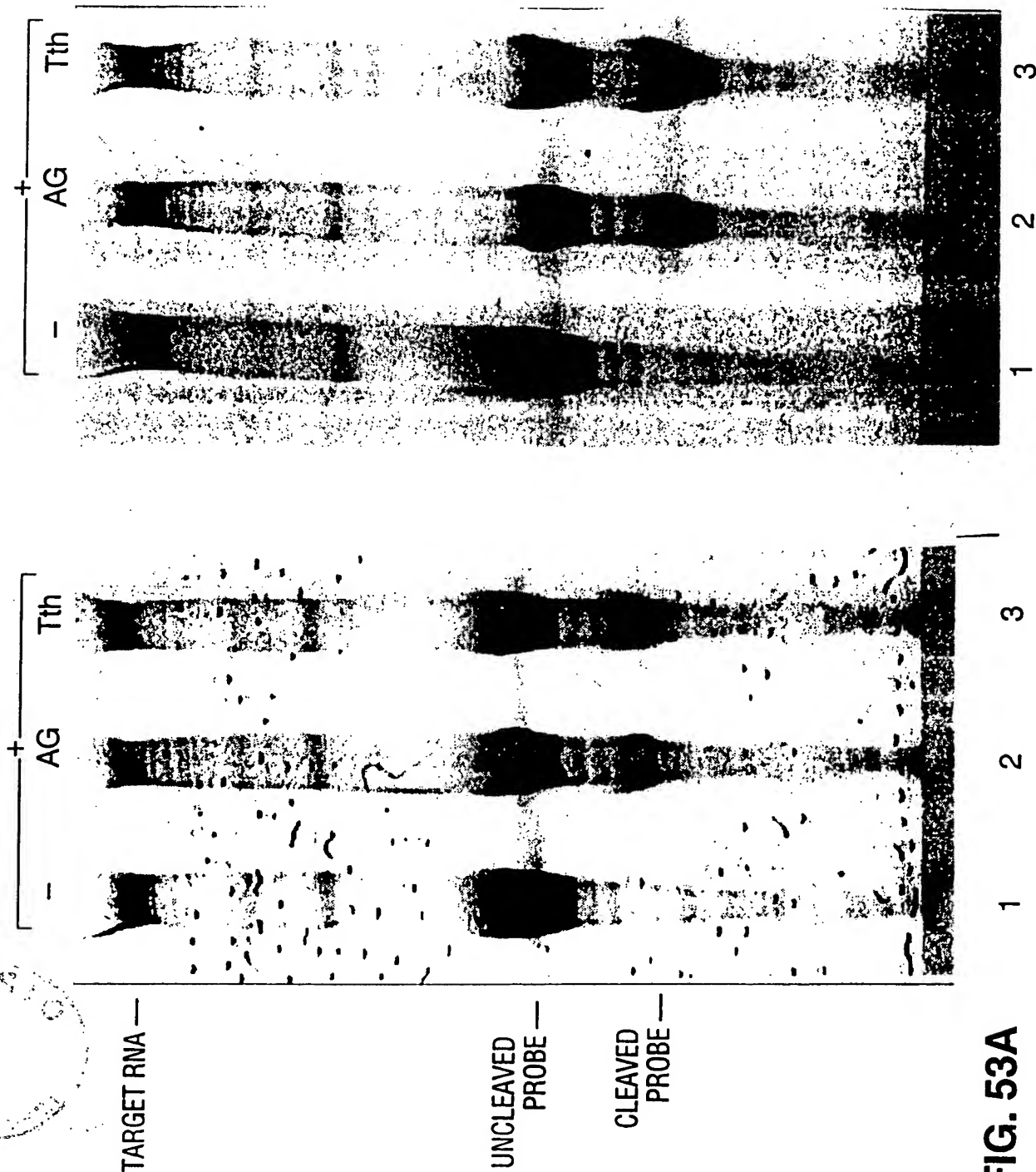


FIG. 53A

FIG. 53B

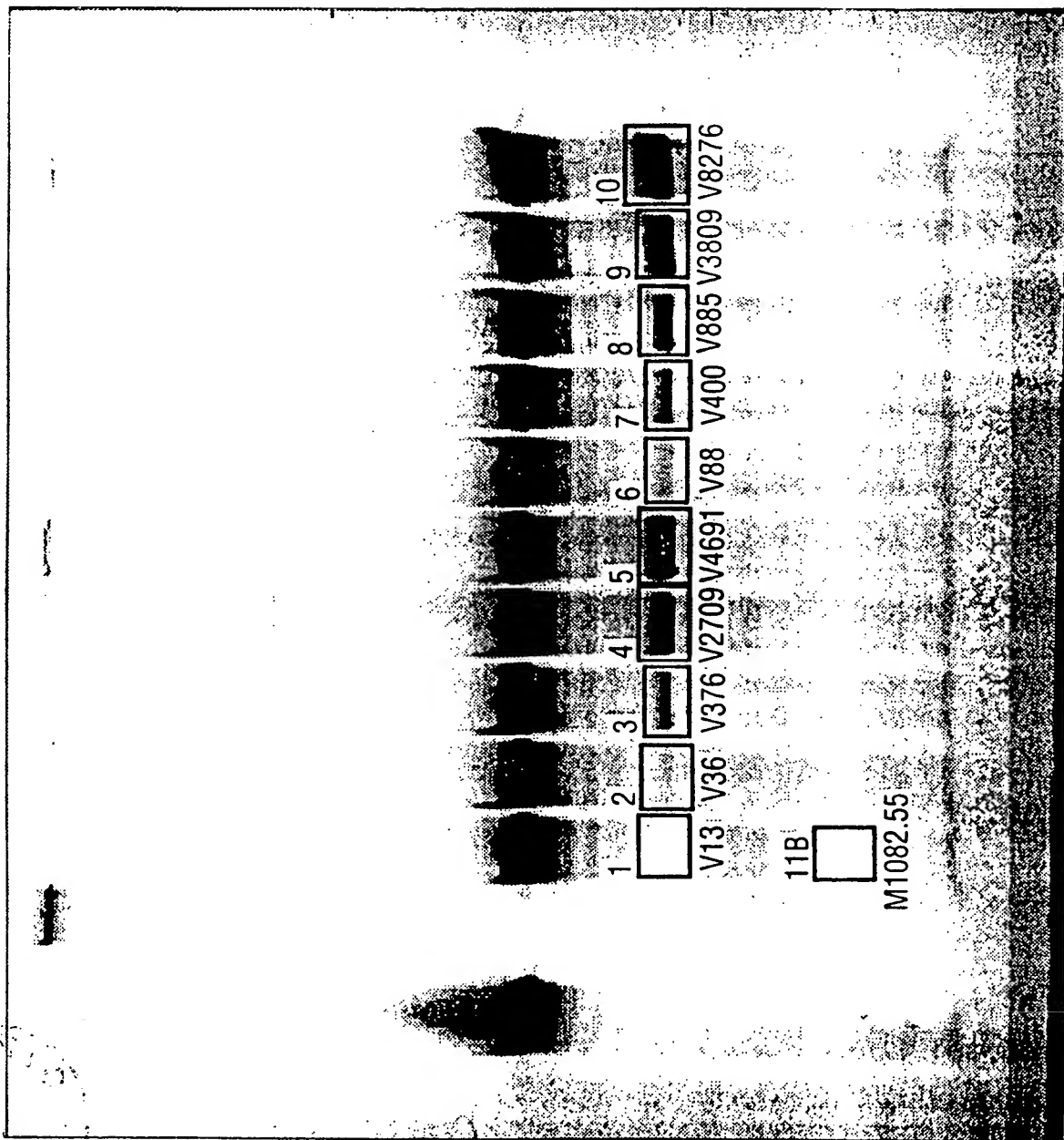
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— ENZYME
— TARGET (fmol)
— RNA

500 1 5 10 50 100 100 10 5 10 50 100

CLEAVASE AG

Tth



— PROBE

— PRODUCT

FIG. 54

10081806.060702

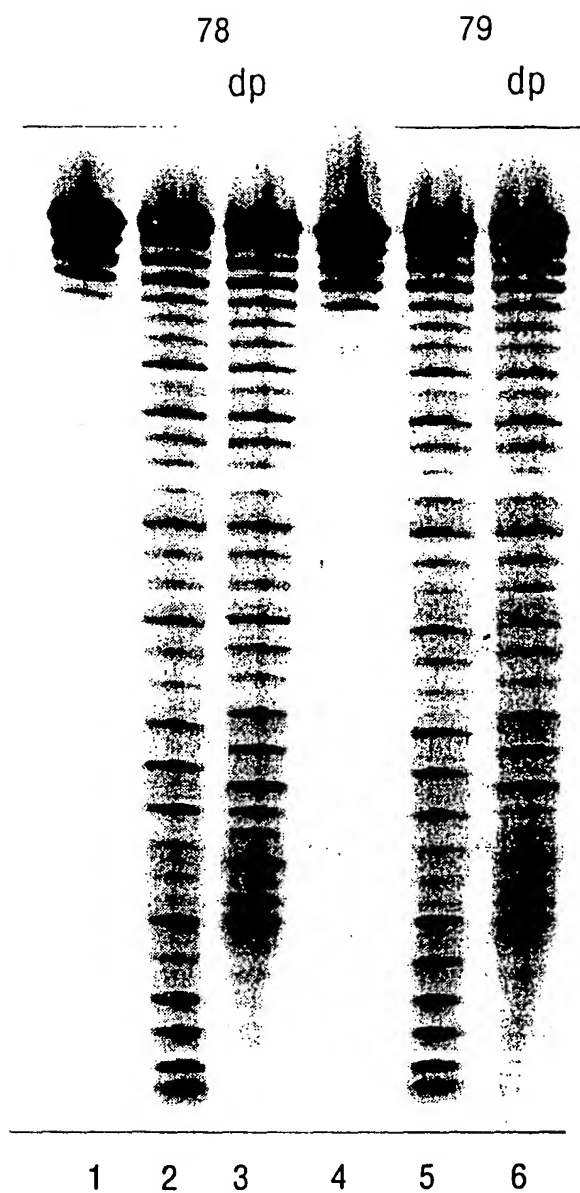


FIG. 55



FIG. 56

FIG. 56

75

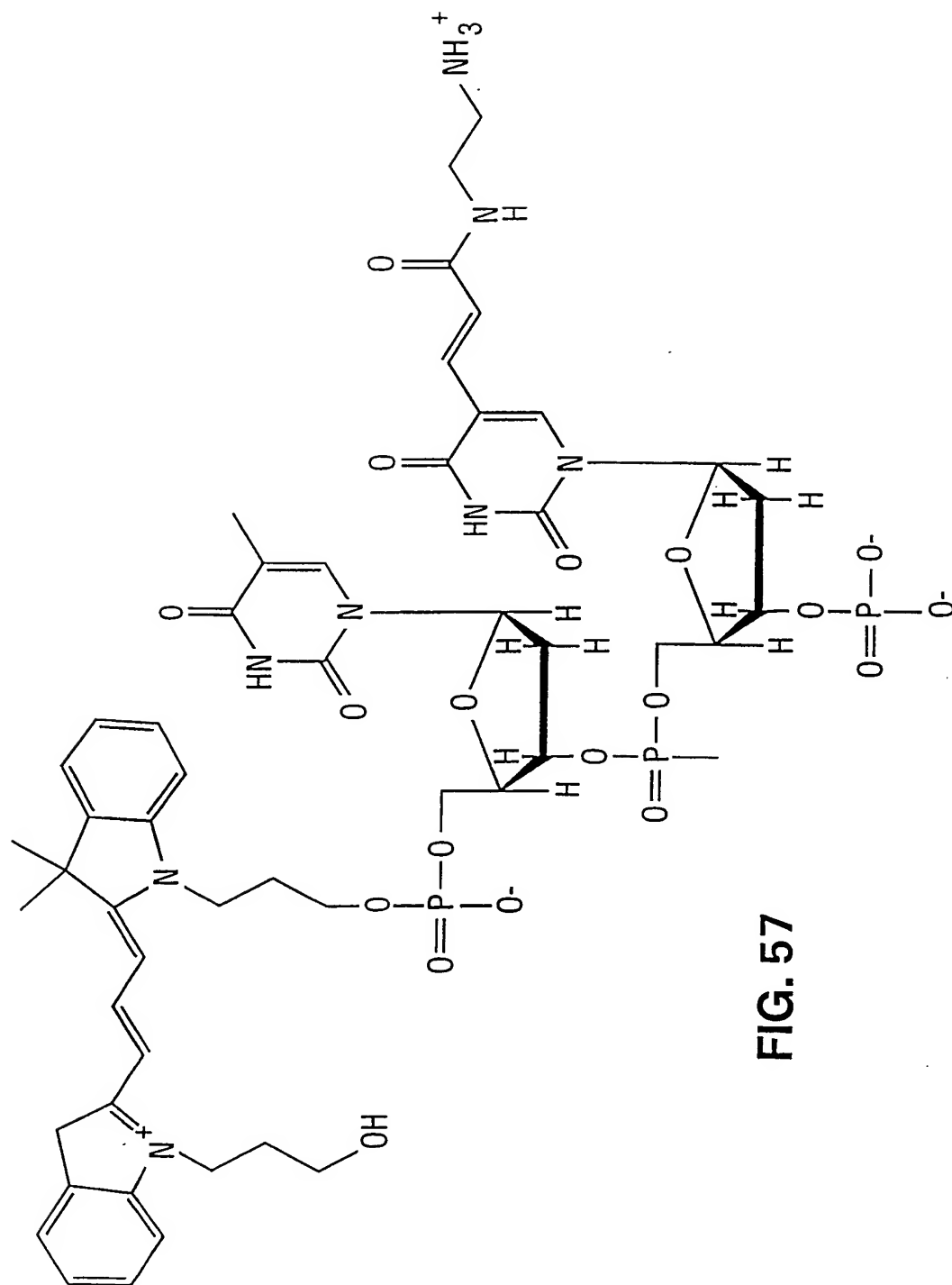


FIG. 57

76

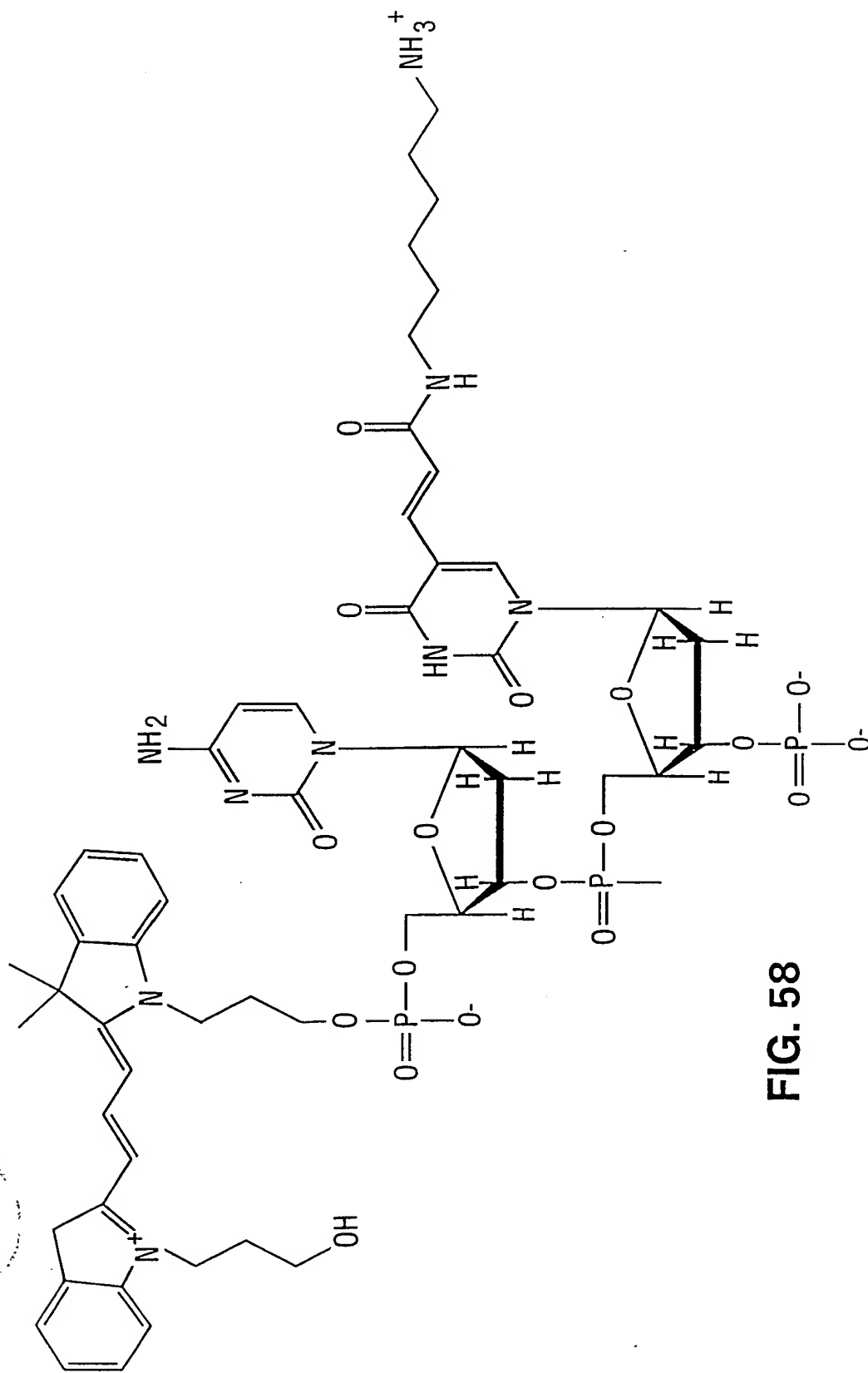


FIG. 58

10084806 060702

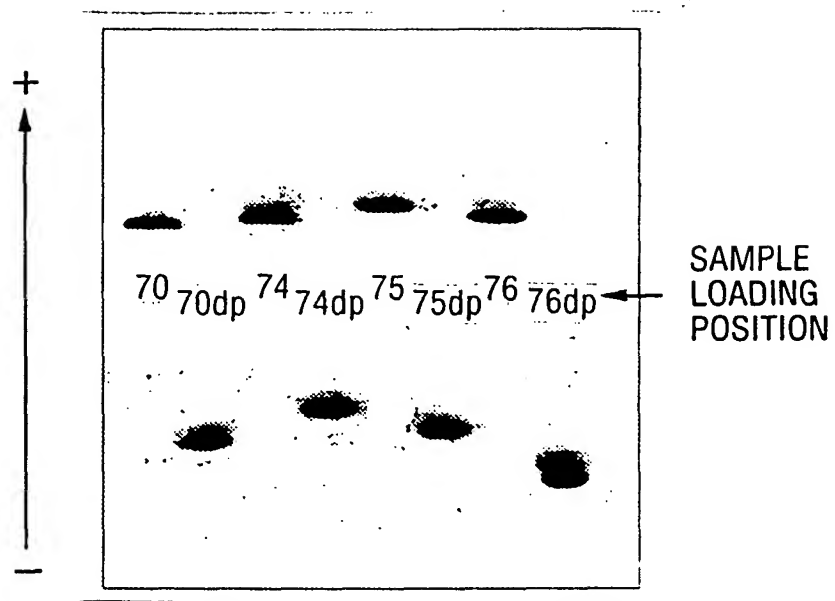


FIG. 59



10081806.060702

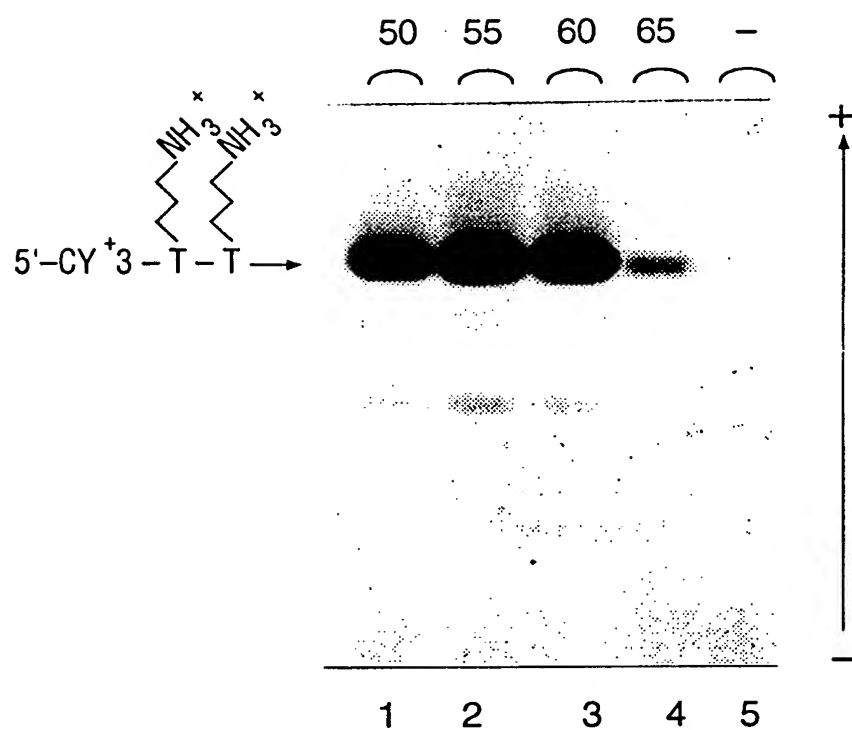


FIG. 60B

10081805-060702

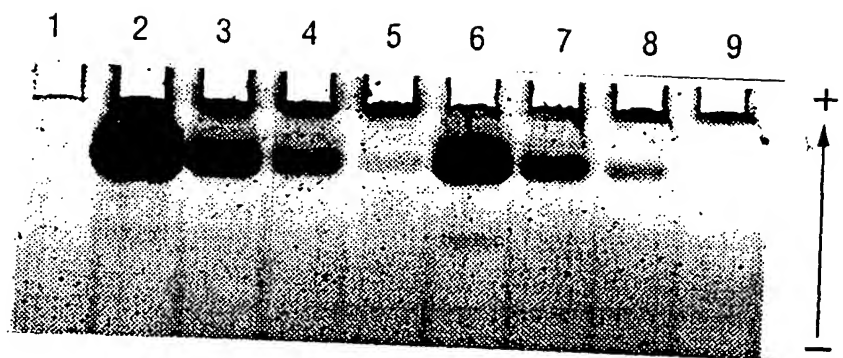
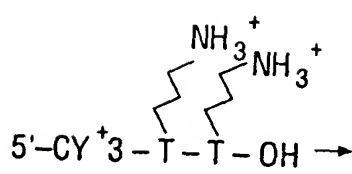


FIG. 61

10081645, 060702

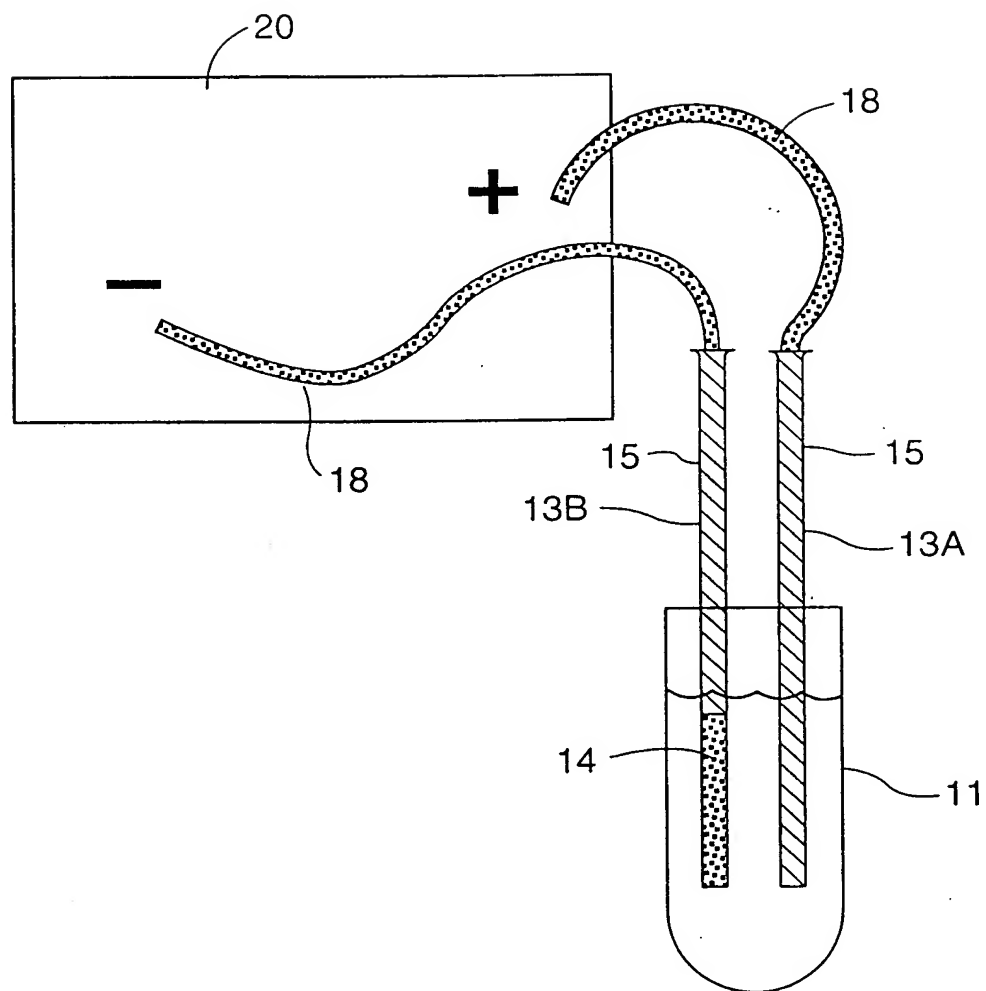


FIG. 62



20100907 90815001

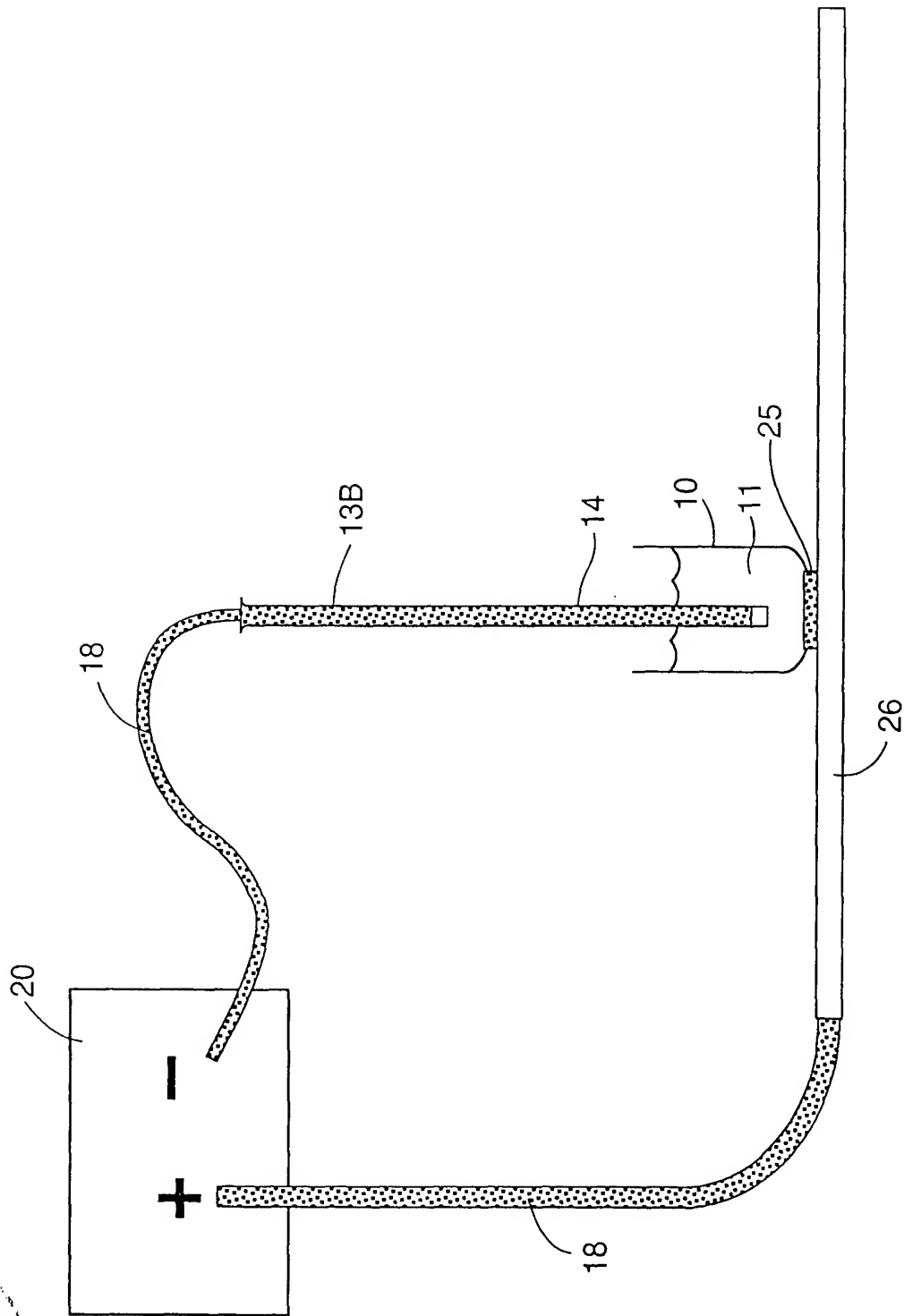


FIG. 63

1081866.060700

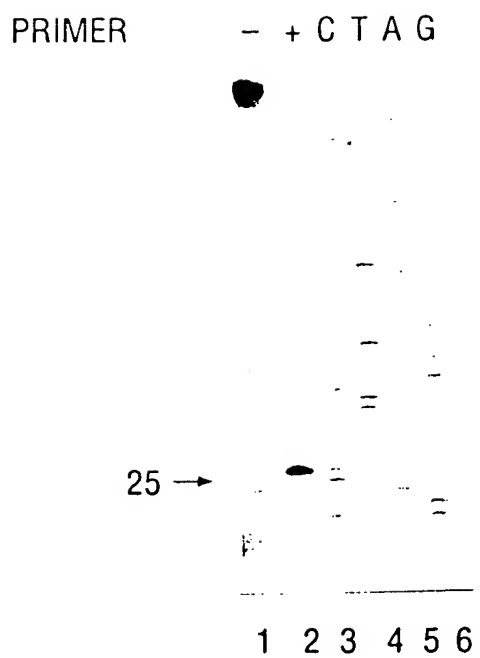


FIG. 64





FIG. 65A



FIG. 65B

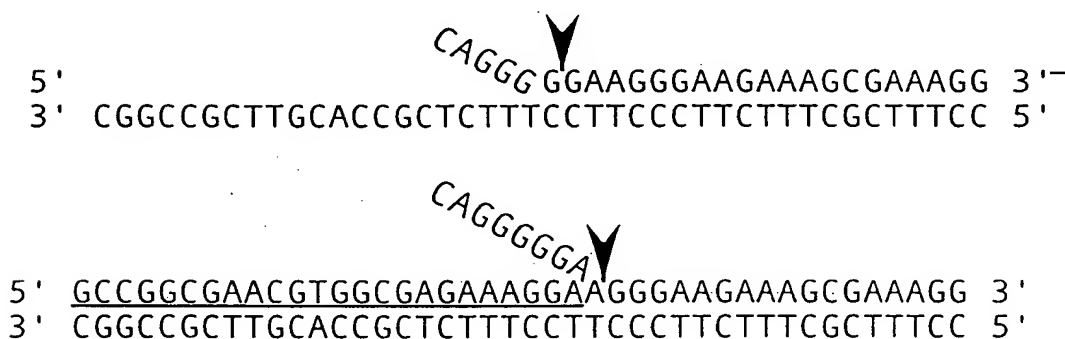


FIG. 65C



FIG. 65D

10091505.066703

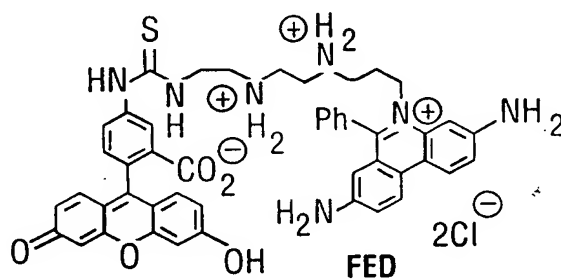
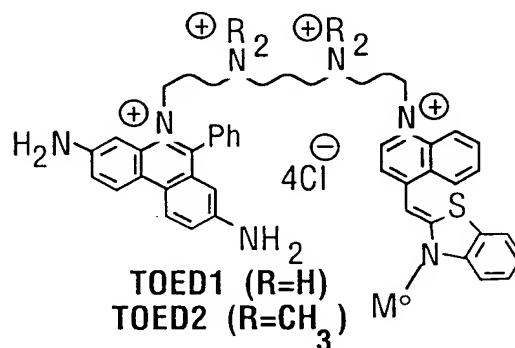
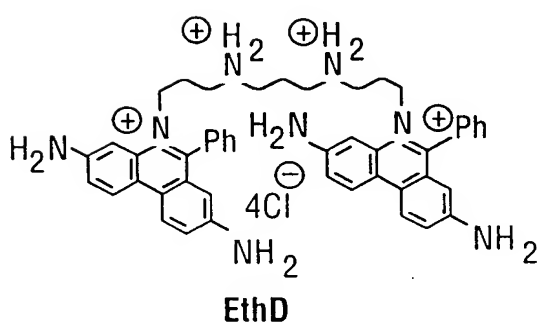
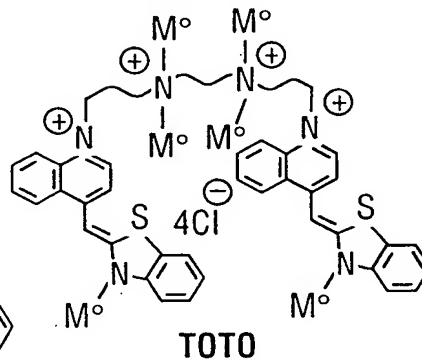
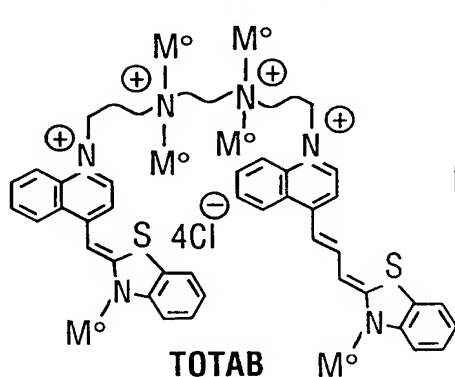
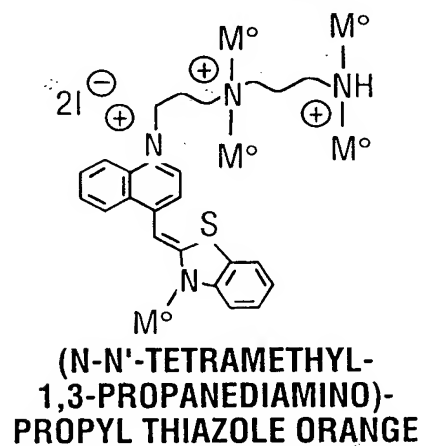
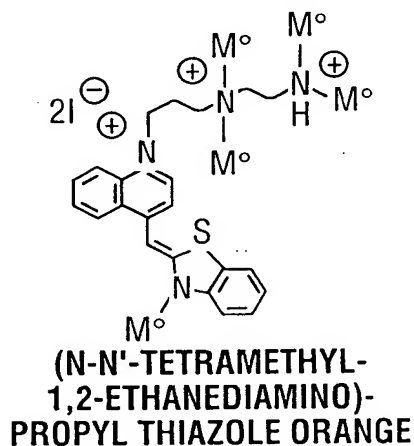
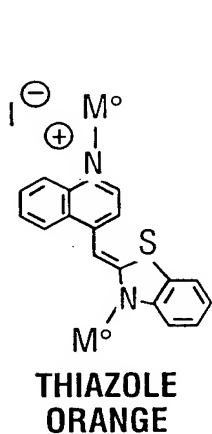
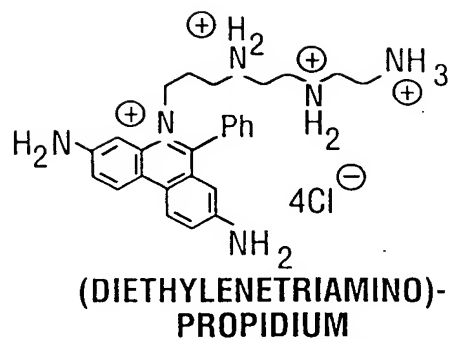
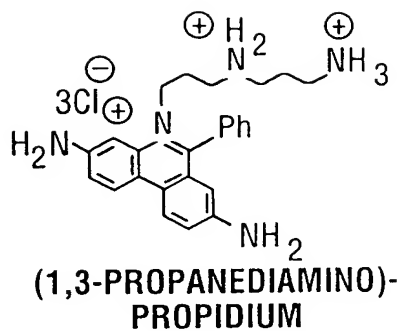
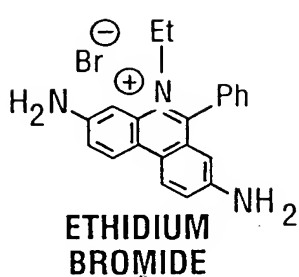


FIG. 66

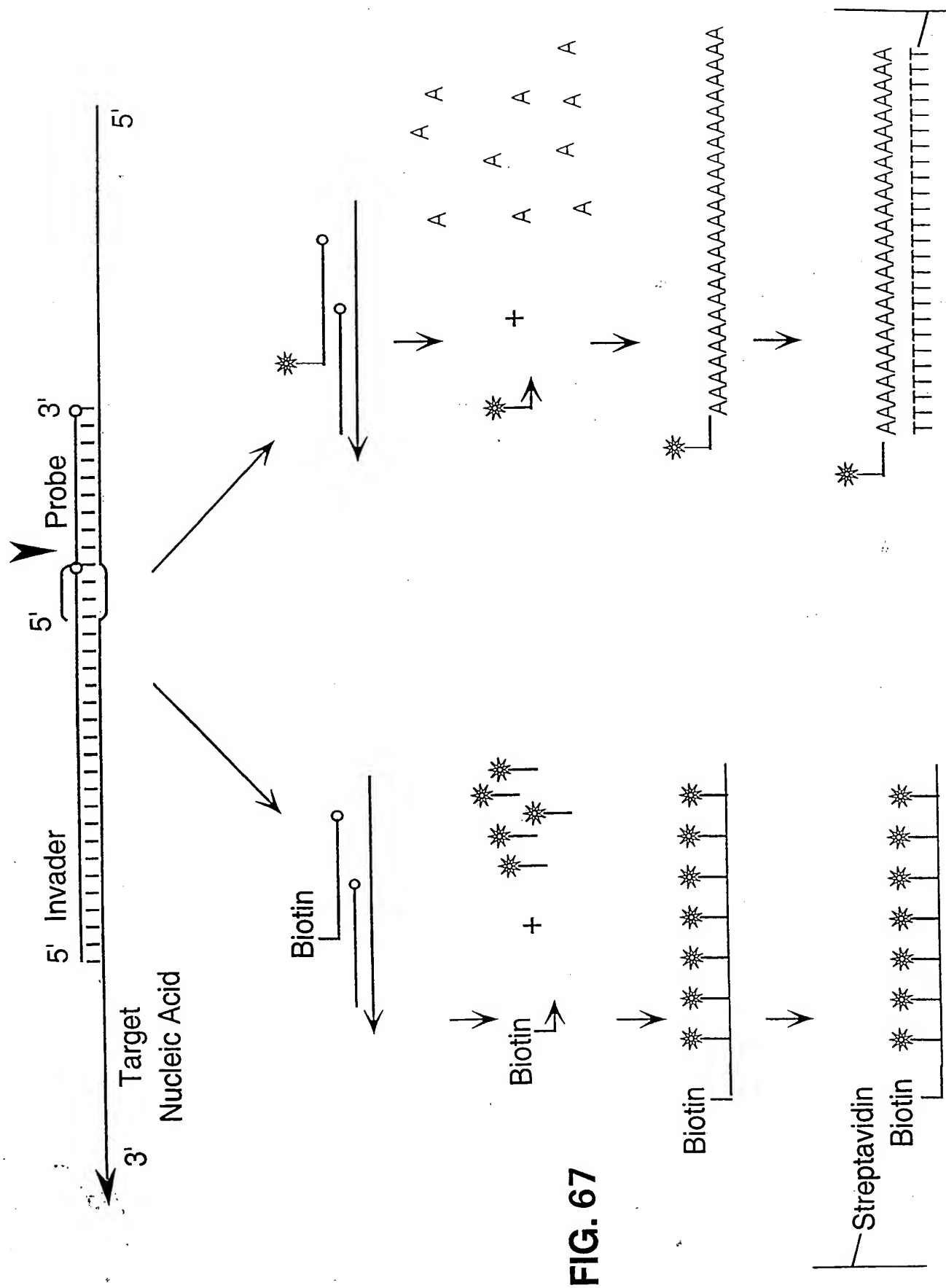


FIG. 67

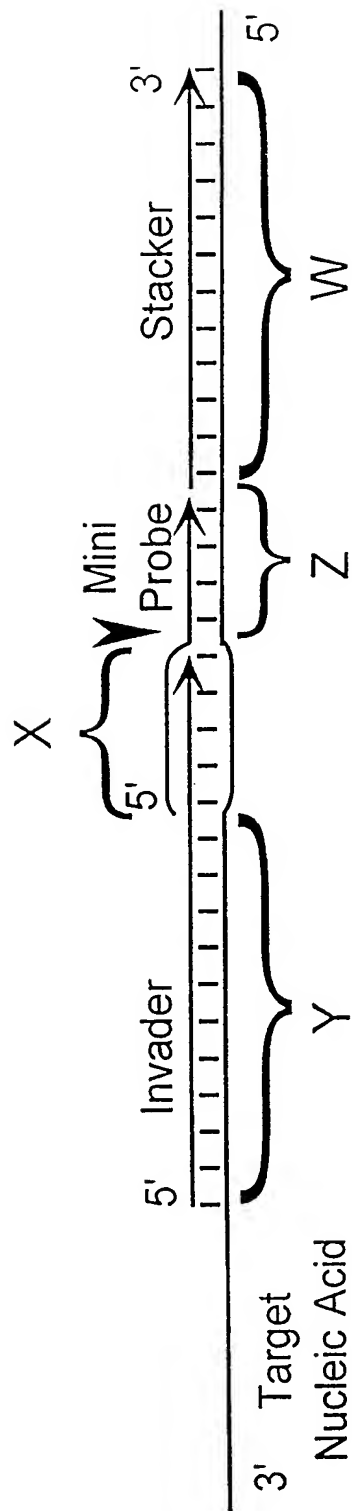


FIG. 68

10081806.060702



FIG. 69



204090" 999T800T

| | 10 | 20 | 30 | 40 | 50 | 60 | 70 | | | | | |
|----|-----------|-------------------|-------------------------|--------------------------------|------------------------|-------------------|------------------------|--------------------|-------------|---------|--------------|------------|
| 1 | MGVQ----- | FGDFIPK-- | NIISFEDL | KGKKVAID | GMNALYQ | FLTSIRLR | DGSPLNRKGEITSAYNGVFY | MJAFEN1.PRO | | | | |
| 1 | MGVP----- | IGEIIPR-- | KEIELENL | YGKKIAID | ALNAIYQ | FLSTIRQ | KDGTPLMDSKGRITSHLSGLFY | PFUFEN1.PRO | | | | |
| 1 | MGIQGLAK | LIADVAPSA | IRENDIKSYFGRKVAID | ASMSIYQFLIAVRQ | -GGDVLQNEEGETTSHLMGMFY | | | HUMFEN1.PRO | | | | |
| 1 | MGIHGLAK | LIADVAPSA | IRENDIKSYFGRKVAID | ASMSIYQFLIAVRQ | -GGDVLQNEEGETTS-LMGMFY | | | MUSFEN1.PRO | | | | |
| 1 | MGIKGLNA | IISEHVPSAIRKSDIKS | FFGRKVAIDASMSLYQFLIAVRQ | QDGGQLTNEAGETTSHLMGMFY | | | | YST510.PRO | | | | |
| 1 | MGVHSFWD | IAG---- | PTARPVRLESLEDK | RMAVDASIWIYQFLKAVRDQ | EGNAVKN----- | SHITGFFR | | YSTRAD2.PRO | | | | |
| 1 | MGVSGLWN | I----- | PVKRPVKLETLV | NKRLAIDASIWIYQFLKAVRDQ | KEGNQLKS----- | SHVVGFFR | | SPORAD13.PRO | | | | |
| 1 | MGVQGLWK | LLE---- | CSGROVSPEALEG | KILAVDISIWLNQALKGVRDRH | NSIEN----- | PHLLTLFH | | HUMXPG.PRO | | | | |
| 1 | MGVQGLWK | LLE---- | CSGHRVSPEALEG | KVLAVDISIWLNQALKGVRDSH | GNVIEN----- | AHLLTLFH | | MUSXPG.PRO | | | | |
| 1 | MGVQGLWK | LLE---- | CSGRP | INPGTLEGKILAVDISIWLNQAVKGARDRQ | GNAIQN----- | AHLLTLFH | | XENXPG.PRO | | | | |
| 1 | MTINGIWE | WANHVV---- | RKVPNETMRD | KTLSIDGHIWLYESLKGCEAHHQ | T----- | PNSYLV | TFFT | CELRAD2.PRO | | | | |
| | 80 | 90 | 100 | 110 | 120 | 130 | 140 | | | | | |
| 64 | KTIHLEND | ITPIWV | FDGEP | PKLKEK | TRKVR | REMKEAELKMKE | AIKK---- | EDFEEAAKYAKRVSYLTP | MJAFEN1.PRO | | | |
| 64 | RTINLME | AGIKPV | YVFDG | EPPEF | KKKE | LEKRREAREE | AEKWR | EALKEK---- | GEIEEARKYAQ | RATRVNE | PFUFEN1.PRO | |
| 70 | RTIRMMEN | GIKPVY | FDGKPP | QLKSGELAKR | SERRAEAEKQLQQA | AA---- | GAEOE | VEKFTKRLVK | VTK | | HUMFEN1.PRO | |
| 69 | RTIRM-EN | GIKPVY | FDGKPP | QLKSGELAKR | SERRAEAEKQLQQA | EA---- | GMEEE | VEKFTKRLVK | VTK | | MUSFEN1.PRO | |
| 71 | RTL | MIDNGIK | PCYV | FDGKPP | DLKSHEL | TKRSSRRVET | EKKLA---- | EA---- | TTELEKM | QERRLVK | VSK | YST510.PRO |
| 61 | RICKLLY | FGIRPV | FVFDG | GVPLKRETI | RQKERRQKRESAK | STARKLLALQLQNGS | NDNKRDS | DEVTM | | | YSTRAD2.PRO | |
| 61 | RICKLLF | FGIKPV | FVFDG | GAPSLKRQTI | QKRQARRLDREENA | TVTANKLLALQMRHQAM | LLKRDA | DEVTQ | | | SPORAD13.PRO | |
| 61 | RLCKLLF | FRIRPI | FVFDG | DAPLLKKQTL | VKRQRKDLASSDSR | KTTTEKLLKTFLKRO | QAIKTER | IAATVTG | | | HUMXPG.PRO | |
| 61 | RLCKLLF | FRIRPI | FVFDG | DAPLLKKQTL | AKRRQRKDSASIDSR | KTTTEKLLKTFLKRO | QALKTDR | IAASVTG | | | MUSXPG.PRO | |
| 61 | RLCKLLF | FRIRPI | FVFDG | EAPLLKKRQT | LAKRRQRTDKASNDARK | TNEKLLRTFLKRO | AIKAER | IAATVTG | | | XENXPG.PRO | |
| 60 | RIQRLL | ELKI | PIVVF | DNINASSA | HESKDQNEFVPR | KRRSFGDS | PTNLV----- | ----- | | | CELRAD2.PRO | |

FIG. 70A

| | 150 | 160 | 170 | 180 | 190 | 200 | 210 |
|-----|---|-----|-----|-----|-----|-----|--------------|
| 130 | KMVENCKYLLSLMGIPYVEAPSEGEAQASYMAKKGDVNAVVSQDYDALYGAPRVVRNLTTTKEM---- | | | | | | MJAFEN1.PRO |
| 130 | MLIEDAKKLLLELMGIPVQAPSEGEAQAAAYMAAKGSVYASASQDYDSLFGAPRLVRNLTTITGKRKLPGK | | | | | | PFUFEN1.PRO |
| 136 | QHNDCKHLLSLMGIPYLDAPSEAEASCAALVKAGKVYAAATEDMDCLTFGSPVLMRHLTASEAKKLP IQ | | | | | | HUMFEN1.PRO |
| 134 | QHNDCKHLLSLMGIPYLDAPSEAEASCAALAKAGKVYAAATEDMDCLTFGSPVLMRHLTASEAKKLP IQ | | | | | | MUSFEN1.PRO |
| 134 | EHNEEAQKLLGLMGIPYIIAPTEAEQAELAKKGVYAAASEMDTLCYRTPFLLRHLTFSEAKKEPIH | | | | | | YST510.PRO |
| 131 | DMIKEVQELLSRFGIPYITAPMEAEQAELQLNLVDGIITDSDVFLFGGKIYKNMFHEKNY---- | | | | | | YSTRAD2.PRO |
| 131 | VMIKECQELRLFGLPYIAPOEAEQAQCSKLELKLVDGIVTDDSDVFLFGGTRVYRNMFNQNKF---- | | | | | | SPORAD13.PRO |
| 131 | QMFLESQELRLFGIPYIQAPMEAEQAQCAILDLTQDTSGITDSDIWLFGARHVYRNFFNKNKF---- | | | | | | HUMXPG.PRO |
| 131 | QMFLESQELRLFGVPYIQAPMEAEAOCAVLDLSDQTSGITDSDIWLFGARHVYKNFFNKNKF---- | | | | | | MUSXPG.PRO |
| 131 | QMCLESQELQLFGIPYIVAPMEAEQAQCAILDLTQDTSGITDSDIWLFGARHVYKNFFSQNKH---- | | | | | | XENXPG.PRO |
| 111 | DHVYKTNALLTELGIKVIAPGDGEAQCARLEQLGVTSGCITTDFDYFLFGGKNLYRFDFTAGT----- | | | | | | CELRAD2.PRO |
| | 220 | 230 | 240 | 250 | 260 | 270 | 280 |
| 195 | -----PELIELNEVLEDLRISLDDLIDIAIFMGTDYNPGGV--K--GIGFKRAYELVRSGVAK--DV | | | | | | MJAFEN1.PRO |
| 200 | NVYVE-IKPELIILEEVVKELKLTREKLIELAILVGTDYNPGGI--K--GIGLKKALEIVRHSKDP LAKF | | | | | | PFUFEN1.PRO |
| 206 | EFHLSRILQELGLNQE QFVDLCIILGSDYCESIRGIGPKRAVDLIQK--HKSIEEIVRRLDPN-----KY | | | | | | HUMFEN1.PRO |
| 204 | EFHLSRVLQELGLNQE QFVDLCIILGSDYCESIRGIGAKRAVDLIQK--HKSIEEIVRRLDPS-----KY | | | | | | MUSFEN1.PRO |
| 204 | EIDTELVRGLDLTIEQFVDLCIMLGCDYCESIRGVGPVTALKIKT--HGSIEKIVEFIESGESNNTKW | | | | | | YST510.PRO |
| 198 | FYDAESILKLLGLDRKNMIELAQLLGSDYTNGLKGMGPVSSIEVIAEF--GNLKNFKDWYNNGOFDK RK | | | | | | YSTRAD2.PRO |
| 198 | LYLMDDMKREFNVNQMDLIKLAHLGSDYTMGLSRVGPVLALEILHEFPDGTGLFEFKKWFQRLSTGHAS | | | | | | SPORAD13.PRO |
| 198 | YYQYVDFHNQGLDRNKLINLAYLLGSDYTEGIP TVGCVTAMEILNEFPGHGLEPLLK FSEWHEAQKNP | | | | | | HUMXPG.PRO |
| 119 | YYQYVDFYSQGLDRNKLINLAYLLGSDYTEGIP TVGCVTAMEILNEFPGRGLDPLLK FSEWHEAQNNK | | | | | | MUSXPG.PRO |
| 198 | YYQYADIHNOGLDRSKLINLAYLLGSDYTEGIP TVGYVSAMEILNEFPGQGLEPLVKFKEWSEAQDK | | | | | | XENXPG.PRO |
| 175 | -----SSTACLHDIMHLSLGRMFM----- | | | | | | CELRAD2.PRO |

FIG. 70B

| | 290 | 300 | 310 | 320 | 330 | 340 | 350 |
|-----|---|----------|----------|----------|----------|----------------------|------------------|
| 251 | LKKEVEYDEIKRIFKEPKV----- | TD-- | NYSLSLKL | PDKEGI | IKFLVD | ENDFN | YD MJAFEN1.PRO |
| 265 | QKQSDVDLYAIKEFFLNPPV----- | TD-- | NYNLVWRD | PDEEGIL | KFLCDE | HDFSEE | PFUFEN1.PRO |
| 269 | PVPENWLHKEAHQLFLEPEV----- | LD | PESVELKW | SEPNEEEL | IKFMCGE | KQFSEE | HUMFEN1.PRO |
| 267 | PVPENWLHKEAQQFLFLEPEV----- | VD | PESVELKW | SEPNEEEL | VKFCMCGE | KQFSEE | MUSFEN1.PRO |
| 272 | KIPEDWPYKQARMFLDPEV----- | ID | NEINLKW | SPPEKE | ELIEYL | CDDKKFSEE | YST510.PRO |
| 265 | QETENKFEKDLRKKLVNNEIILDDDFSPVMVYDAYMRPEVDHDTT | PFVW | GV | PD | DLMLRS | FMKTQLGWPHE | YSTRAD2.PRO |
| 268 | KNDVNTPVKKRINKLVGK-IILPSEFPNPLVDEAYLHPAVDDSKQSFQW | GIPDL | DEL | RQFL | MATV | GW | SKQ SPORAD13.PRO |
| 268 | KIRPNPHDTKVKKKL--RTLQLTPGFNP | PAVAEAYL | KPVVDD | SKGS | FLWG | KPDLDKIREFCORYFGWNRT | HUMXPG.PRO |
| 268 | KVAENPYDTKVKKKL--RKLQLTPGFNP | PAVADAYL | RPVVDD | SRGS | FLWG | KPDVDKIREFCORYFGWNRM | MUSXPG.PRO |
| 268 | KMRPNPNDTKVKKKL--RLDLQQSFPN | PAVASAYL | KPVVDE | SKSA | FSWGR | PDLEQIREFCESRFGWYRL | XENXPG.PRO |
| 194 | -----EKKVSRPHLISTAILLGCDYFORGVQ | NI | GIVSVF | -ILGE | FDDG | NEEIDPHVILDRFASYVRE | CELRAD2.PRO |

| | 360 | 370 | 380 | 390 | 400 | 410 | 420 | |
|-----|--------------------------|-----------|----------|--------|-------|--------|-----------------|---|
| 300 | RVKKHVDKLYNLIA----- | | | | | | MJAFEN1.PRO | |
| 314 | RVKNGLERLKKAI----- | | | | | | PFUFEN1.PRO | |
| 320 | RIRSGVKRLSKSRQGS-TQGR | LDDFFKVT | | | | | HUMFEN1.PRO | |
| 318 | RIRSGVKRLSKSRQGS-TQGR | LDDFFKVT | | | | | MUSFEN1.PRO | |
| 323 | RVKSGISRLKKGLKSG-IQGR | LDDGFFOVV | | | | | YST510.PRO | |
| 335 | KSDEILILIRDVNKRKK----- | | | | | KGKQ | YSTRAD2.PRO | |
| 337 | RTNEVLLPVIQDMHKKOF----- | | | | | VG | TQ SPORAD13.PRO | |
| 336 | KTDESIFPVLKQLDAQQTQLRIDS | FFRLAQ | QEKEDAK | RIKSQ | RNLRA | VTCMLR | KEKEAA | SEIEAVSVAM HUMXPG.PRO |
| 336 | KTDESLYPVLKHLNAHQTLRIDS | FFRLAQ | QEKQDA | KLIKSH | RLSRA | VTCMLR | KERE | EKAPELTKVTEAM MUSXPG.PRO |
| 336 | KTDEVLLPVLKQLNAQQTQLRIDS | FFRLAQ | QHEAAG-- | --LKS | QRLRA | VTCMLR | KERD | VEAEEVEAAVAM XENXPG.PRO |
| 257 | EIPARSED | TQ | RKLRLRR | KKYNFP | VGFP | NCDA | VHNAIT | MYLRPPVSSEIPKIIPR-----AANFQQVAEIM CELRAD2.PRO |

FIG. 70C

| | 430 | 440 | 450 | 460 | 470 | 480 | 490 |
|-----|-------|-------|-------|-------|-------|-------|--------------|
| 314 | ----- | ----- | ----- | ----- | ----- | ----- | MJAFEN1.PRO |
| 327 | ----- | ----- | ----- | ----- | ----- | ----- | PFUFEN1.PRO |
| 348 | ----- | ----- | ----- | ----- | ----- | ----- | HUMFEN1.PRO |
| 346 | ----- | ----- | ----- | ----- | ----- | ----- | MUSFEN1.PRO |
| 351 | ----- | ----- | ----- | ----- | ----- | ----- | YST510.PRO |
| 357 | ----- | ----- | ----- | ----- | ----- | ----- | YSTRAD2.PRO |
| 359 | ----- | ----- | ----- | ----- | ----- | ----- | SPORAD13.PRO |
| 406 | ----- | ----- | ----- | ----- | ----- | ----- | HUMXPG.PRO |
| 406 | ----- | ----- | ----- | ----- | ----- | ----- | MUSXPG.PRO |
| 403 | ----- | ----- | ----- | ----- | ----- | ----- | XENXPG.PRO |
| 322 | ----- | ----- | ----- | ----- | ----- | ----- | CELRAD2.PRO |

| | 500 | 510 | 520 | 530 | 540 | 550 | 560 |
|-----|-------|-------|-------|-------|-------|-------|------------------------|
| 314 | ----- | ----- | ----- | ----- | ----- | ----- | NKTKQKTL MJAFEN1.PRO |
| 327 | ----- | ----- | ----- | ----- | ----- | ----- | KSGKQSTL PFUFEN1.PRO |
| 352 | ----- | ----- | ----- | ----- | ----- | ----- | KKKAKTGAAG HUMFEN1.PRO |
| 350 | ----- | ----- | ----- | ----- | ----- | ----- | KKKAKTGGAG MUSFEN1.PRO |
| 354 | ----- | ----- | ----- | ----- | ----- | ----- | NKKLNKNK YST510.PRO |
| 364 | ----- | ----- | ----- | ----- | ----- | ----- | YSTRAD2.PRO |
| 429 | ----- | ----- | ----- | ----- | ----- | ----- | SPORAD13.PRO |
| 476 | ----- | ----- | ----- | ----- | ----- | ----- | HUMXPG.PRO |
| 469 | ----- | ----- | ----- | ----- | ----- | ----- | MUSXPG.PRO |
| 458 | ----- | ----- | ----- | ----- | ----- | ----- | XENXPG.PRO |
| 387 | ----- | ----- | ----- | ----- | ----- | ----- | CELRAD2.PRO |

FIG. 70D

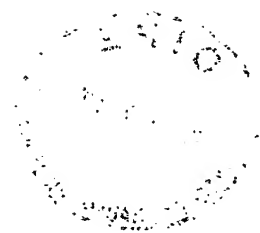
204090" 90848004

322 DAWFKZ
335 ESWFKR
375 KFKRGK
373 KFRRGK
377 VTKGRR
390 ---RKM
483 SKRRRK
546 RKRKTZ
538 RRKKKT
523 TVKRK
429 ELGDSD

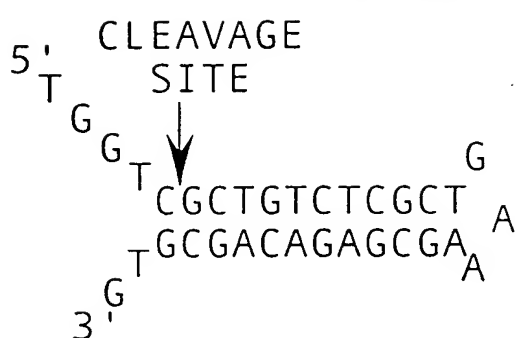
MJAFEN1.PRO
PFUFEN1.PRO
HUMFEN1.PRO
MUSFEN1.PRO
YST510.PRO
YSTRAD2.PRO
SPORAD13.PRO
HUMXPG.PRO
MUSXPG.PRO
XENXPG.PRO
CELRAD2.PRO

FIG. 70E

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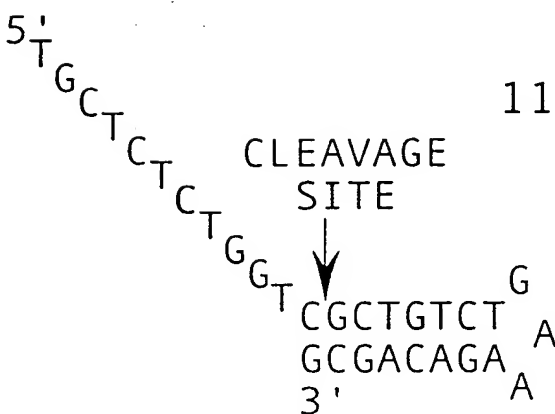


FIG. 71